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(54) **Sulfamoyl-substituted phenethylamine derivatives, their preparation, and pharmaceutical compositions, containing them.**

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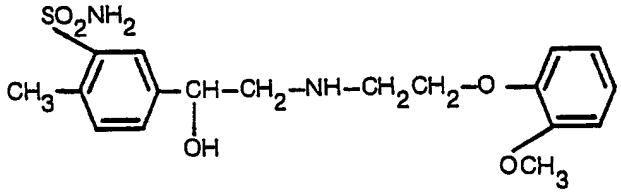
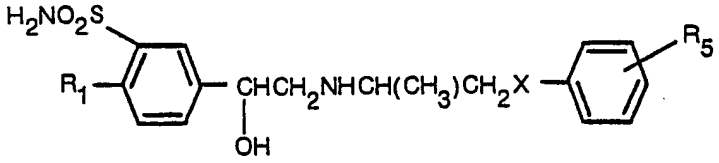
Sulfamoyl-substituted phenethylamine derivatives, their preparation, and pharmaceutical compositions, containing them

This invention relates to sulfamoyl-substituted phenethylamine derivatives and acid addition salts thereof, their preparation, and their pharmaceutical use. Compounds according to the invention exhibit α-adrenergic blocking action and can be used as antihypertensive agents and for treating congestive heart failure.

British Patent No. 2,006,772 discloses a series of compounds exhibiting α- and β-adrenergic blocking actions and that the compound shown by the following formula exhibits strong α- and β-adrenergic blocking actions

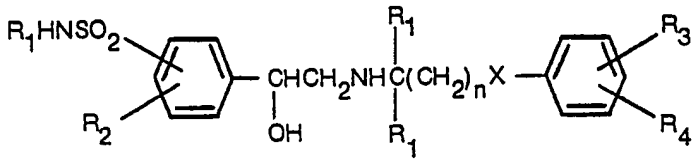


U.S. Patent No. 4,140,713 discloses a series of phenylethanolamine compounds represented by the general formula:



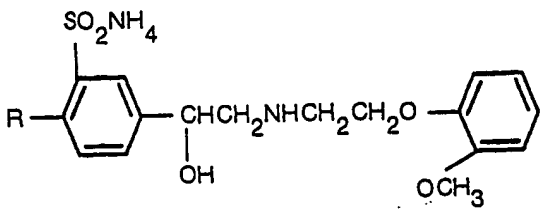
wherein R_1 is a halogen atom or a group NR_2R_3; R_2 and R_3 are the same or different and are hydrogen or a C_1 to C_6 straight or branched chain alkyl group or may together with the nitrogen atom form a 5 or 6 membered heterocyclic ring which may contain a further hetero atom selected from O, N or S; or R_2 may be hydrogen and R_3 may be the group R_4CO or R_4SO_4 where R_4 is hydrogen or a C_1 to C_4 alkyl group; R_5 is hydrogen or one or more halogen atoms or hydroxy or C_1 to C_4 alkoxy groups; and X is CH_2O or a group NR_6 where R_6 is hydrogen or a C_1 to C_4 alkyl group. These compounds are said to block β-adrenoreceptors.

Japanese Patent Application No. 53—128098 discloses phenylethanolamine derivatives represented by the general formula:



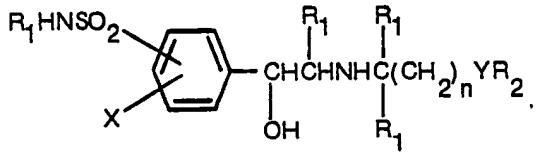
wherein R_1 is hydrogen or a lower alkyl group; R_2 and R_4 are hydrogen, a hydroxy group, a lower alkoxy group or hafogen; R_3 is a lower alkenyl, alkenyloxy or alkenylcarbonyl group; n is 0, 1 or 2 and X is oxygen, sulphur or a methylene group. These compounds show both α and β adrenergic blocking activity.

Japanese Patent Application No. 53—148862 discloses phenylethanolamine derivatives represented by the general formula:



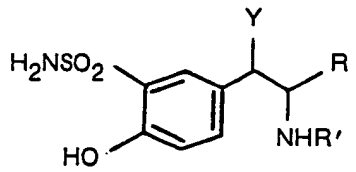
wherein R is a methyl or methoxy group. These compounds act as amphiblockers for α and β receptors.

Japanese Patent Application No. 53—128099 discloses phenylethanolamine derivatives represented by the general formula:



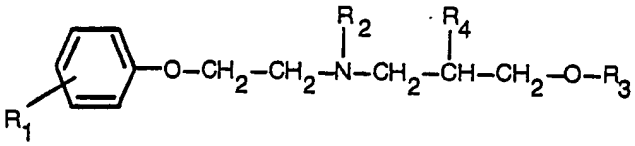
wherein X is hydrogen, a lower alkyl or alkoxy group, halogen, or a hydroxy, sulphamoyl, carbamoyl or cyano group; R_1 is hydrogen or a lower alkyl group; n is 0, 1 or 3; Y is oxygen, sulphur or a methylene group; and R_2 is a (substituted) aryl group or benzodioxane ring. These compounds have α and β blocking activity.

U.S. Patent No. 3,860,647 discloses a series of compounds shown by the following general formula



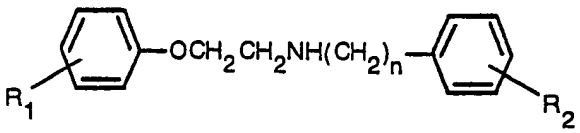
wherein R represents hydrogen or alkyl having 1—4 carbon atoms; R′ represents alkyl having 1—6 carbon atoms, cycloalkyl having 3—6 carbon atoms, $XC_6H_4(CH_2)_2CH(CH_3)$, $XC_6H_4(CH_2)_2C(CH_3)_2$, $XC_6H_4CH_2CH(CH_3)$, or $XC_6H_4CH_2C(CH_3)_2$ (wherein X represents hydrogen, hydroxyl or methoxy); and Y represents hydrogen or hydroxy. It is disclosed in this U.S. Patent that these compounds exhibit β-adrenergic blocking action.

British Patent No. 902,617 discloses a series of compounds shown by the following general formula



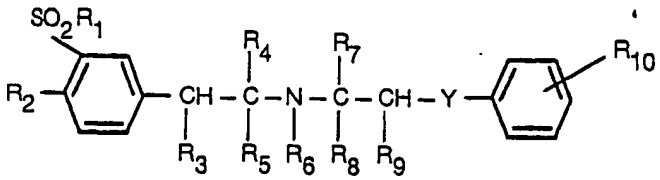
wherein R_1 is hydroxyl, methyl, methoxy, etc.; R_2 is hydrogen, methyl, etc.; R_3 is phenyl, benzyl or a hydroxy-, methyl-, methoxy-, ethoxy-, chloro- or bromo-substituted phenyl or benzyl radical, etc.; and R_4 is hydrogen, etc. These compounds exhibit α-adrenergic blocking action (see, "J. Med. Chem."; *9*, 812—818 (1966)) and possess antihypertensive activity.

Also, in "J. Med. Chem."; *9*, 812—818 (1966), it is disclosed that the phenoxyethylamine-type compounds shown by the following general formula possess α-adrenergic blocking action



wherein R_1 represents *o*-OCH_3, etc., and R_2 represents *o*- or *p*-OCH_3, etc.

According to this invention there are provided sulfamoyl-substituted phenethylamine derivatives shown by following general formula I:



I

wherein R_1 represents an amino group or a mono- or di-lower alkylamino group; R_2 represents a hydroxyl group, a lower alkyl group, or a lower alkoxy group; R_3 represents hydrogen, halogen, a lower alkyl group, a lower alkoxy group, a phenylthio group, or a phenylsulfinyl group; R_4, R_5, R_6, R_7, R_8 and R_9 are selected independently from hydrogen and lower alkyl groups; R_{10} represents hydrogen, a lower alkyl group, or a lower alkoxy group; and Y represents oxygen or a methylene group with the provisos that Y is oxygen when R_2 is a hydroxyl group, and R_1 is NH_2, R_2 is a lower alkyl group, R_3, R_4, R_5, R_6, R_7

and R_9 are hydrogen, R_8 is a lower alkyl group and R_{10} a lower alkoxy group when Y is a methylene group; or a salt thereof.

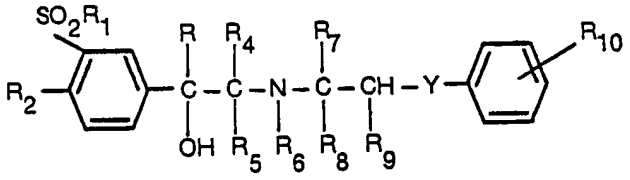
The term "lower" used herein means a straight or branched carbon chain having 1 to 5 carbon atoms. For example, "lower alkyl group" includes methyl, ethyl, propyl, butyl, pentyl and isobutyl groups, etc.; and "lower alkoxy group" includes methoxy, ethoxy, propoxy and butoxy groups, etc. Also, in the above-described formula, R_{10} which is a substituent of the benzene ring may be disposed at any position *ortho-*, *meta-* or *para-*to the side chain. Furthermore, since the compounds of this invention shown by formula I can readily form salts and contain asymmetric carbon atom(s), the invention includes the salts thereof, and any optically active or inactive isomer or isomer mixture thereof.

The compounds of the present invention exhibit α- adrenergic blocking action and thus can be utilized for various treatments. For example, they can be used for the treatment of hypertension, congestive heart failure, angina pectoris, lower urinary tract dysfunction, prostatic hypertrophy, pheochromocytoma and peripheral vascular disorders.

The compounds of this invention shown by formula I can be produced by the following processes.

Process 1:

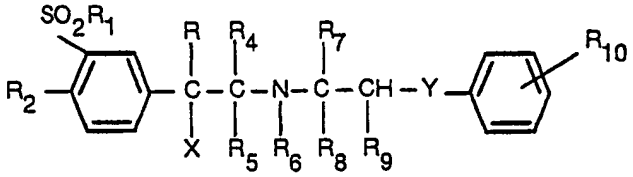
A compound of formula I is obtainable by reacting a compound shown by general formula II



II

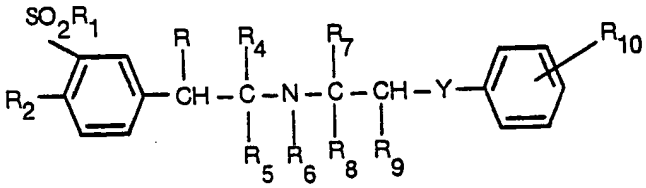
wherein R represents hydrogen or a lower alkyl group and R_1, R_2, R_4, R_5, R_6, R_7, R_8, R_9, R_{10} and Y have the same significance as in formula I with halogenating agent and then, if desired, (a) reducing the halogenated product obtained by the above reaction; or (b) reacting the halogenated product with alkaline material and then reacting the product thus obtained with hydrogen iodide, a lower alcohol, or thiophenol, and further, if desired, oxidizing the product obtained by the reaction with thiophenol.

In process I a starting material shown by formula II described above can be reacted with halogenating agent to provide a product shown by general formula I_1



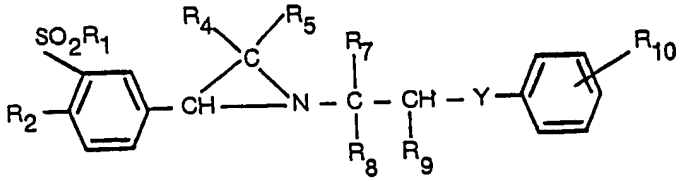
I_1

wherein X represents chlorine or bromine and R, R_1, R_2, R_4, R_5, R_6, R_7, R_8, R_9, R_{10} and Y have the same significance as in formula II and then, if desired, (a) the halogenated product shown by formula I_1 is reduced to form a compound shown by formula I_2



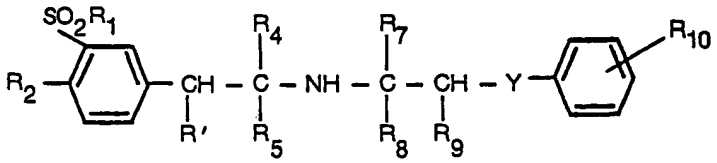
I_2

wherein R, R_1, R_2, R_4, R_5, R_6, R_7, R_8, R_9, R_{10} and Y have the same significance as above described; or (b) the halogenated product shown by formula I_1 is treated with alkaline material to form the aziridine compound shown by following general formula III



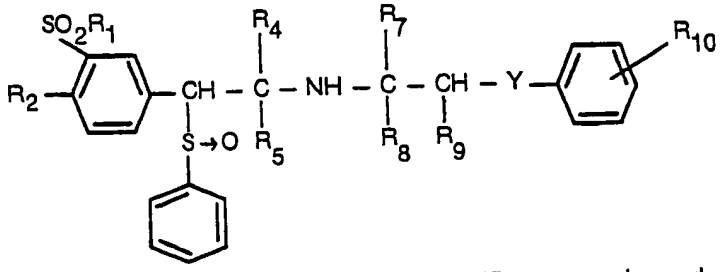
III

wherein R_1, R_2, R_4, R_5, R_7, R_8, R_9, R_{10} and Y have the same significance as above described, and then the aziridine compound is reacted with hydrogen iodide, a lower alcohol, or thiophenol to provide the compound shown by general formula I_3



I_3

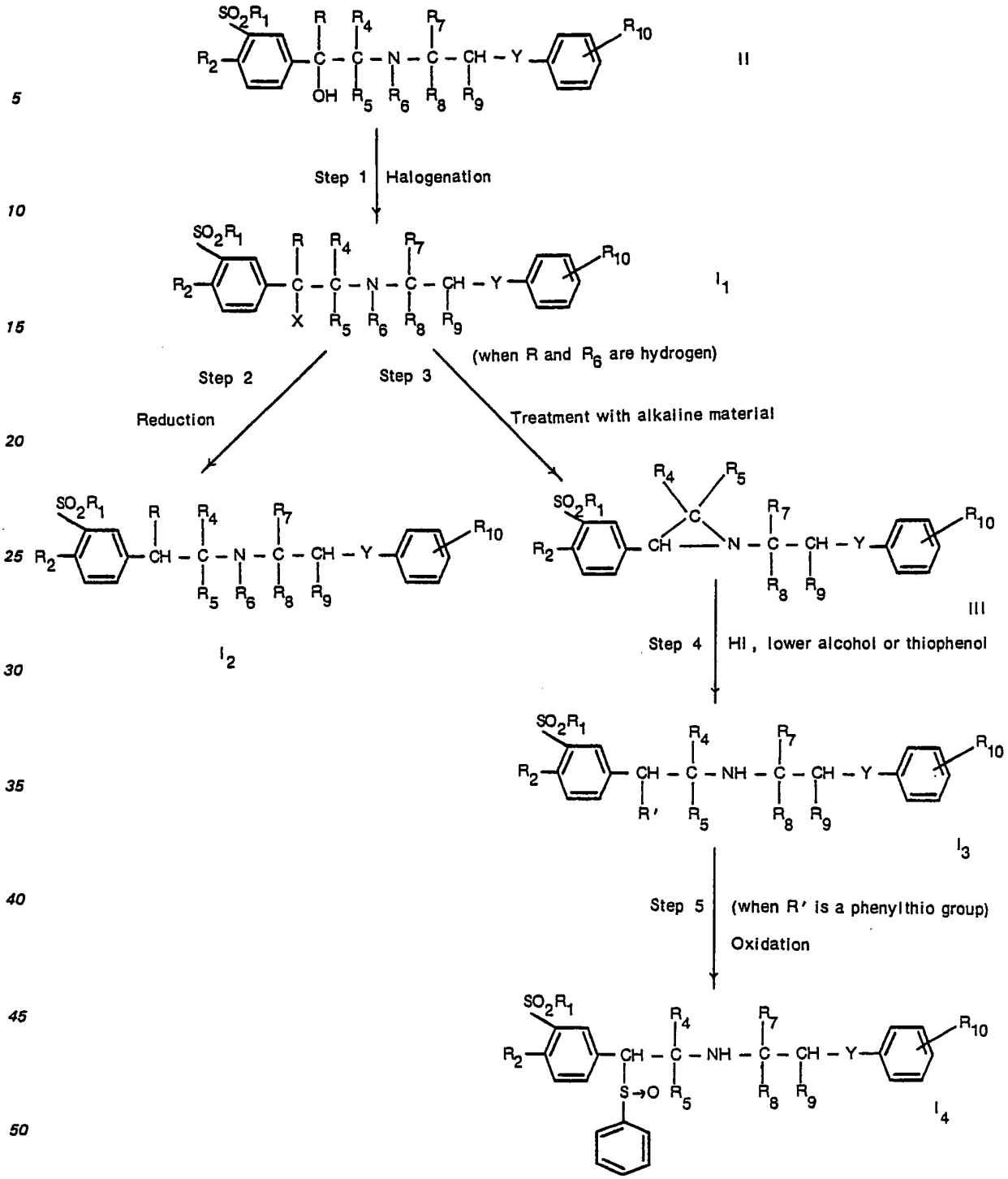
wherein R′ represents iodine, a lower alkoxy group or a phenylthio group and R_1, R_2, R_4, R_5, R_7, R_8, R_9, R_{10} and Y have the same significance as above described; further, when R′ of the compound shown by formula I_3 is a phenylthio group the compound can be oxidized to provide the compound shown by general formula I_4



I_4

wherein R_1, R_2, R_4, R_5, R_7, R_8, R_9, R_{10} and Y have the same significance as above described.

This process is further schematically shown below, the compounds shown by formulae I_1, I_2, I_3 and I_4 being compounds according to this invention.



The reaction conditions in the steps described above may be as follows:

Step 1:

The halogenation of the compounds of formula II can be performed in an organic solvent such as toluene, methyl ethyl ketone, acetonitrile, tetrahydrofuran, etc., at room temperature or under heating using a halogenating agent such as thionyl chloride, hydrogen chloride, hydrogen bromide, phosphorus trichloride, phosphorus pentachloride, phosphorus oxychloride, thionyl bromide, etc.

Step 2:

The reduction of the compounds of formula I_1 can be performed in an organic solvent such as methanol, ethanol, toluene, acetonitrile, tetrahydrofuran, etc., under hydrogen stream, at normal temperature and normal pressure using a catalyst such as platinum oxide, palladium carbon, etc.

Step 3:

The compounds of formula III can be obtained by treating the compounds of formula I_1 (wherein, however, R and R_6 are hydrogen) with an alkaline material such as sodium carbonate, metal alcoholate, sodium hydroxide, potassium hydroxide, etc., in an organic solvent such as ethyl acetate, ethanol, dioxane, benzene, etc., at room temperature to 50°C.

Step 4:

i) The compounds of formula I_3 (wherein R' is a phenylthio group) can be obtained by reacting the compounds of formula III with thiophenol in an organic solvent such as methanol, chloroform, ethyl acetate, dioxane, benzene, etc., at room temperature.

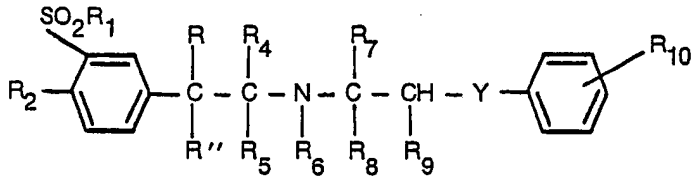
ii): The compounds of formula I_3 (wherein R' is a lower alkoxy group) can be obtained by reacting the compounds of formula III with a lower alcohol in the presence of BF_3 catalyst under the same condition as in the step i).

iii): The compounds of formula I_3 (wherein R' is iodine) can be obtained by reacting the compounds of formula III with hydroiodic acid in an organic solvent such as dioxane, methanol, etc., at room temperature.

Step 5:

The oxidation of the compounds of formula I_3 (wherein R' is a phenylthio group) can be performed in acetic acid at temperatures of 50—60°C using H_2O_2 as the oxidizing agent.

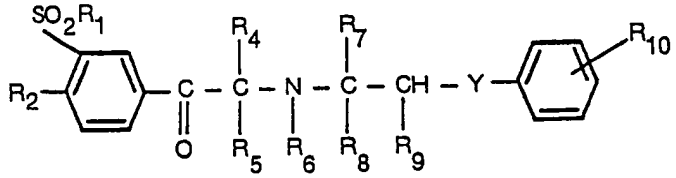
In addition, among the compounds of this invention, the compounds shown by following general formula I_5



I_5

wherein R'' represents a lower alkoxy group or a phenylthio group and R, R_1, R_2, R_4, R_5, R_6, R_7, R_8, R_9, R_{10} and Y have the same significance as above described can be obtained by reacting the compounds of formula I_1 directly with a lower alcohol or thiophenol.

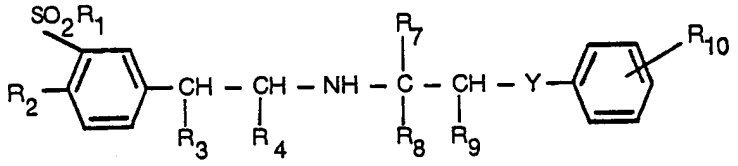
The starting materials of formula II wherein R is hydrogen used in the process of this invention are described in British Patent No. 2,006,772; the starting materials of formula II wherein R is a lower alkyl group can be obtained by reacting the compounds of the following formula



described in the aforesaid British patent with a Grignard reagent (lower alkyl-MgX).

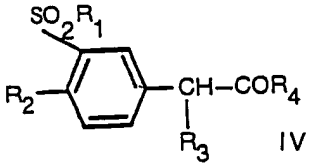
Process 2:

A compound of this invention shown by following general formula I_6



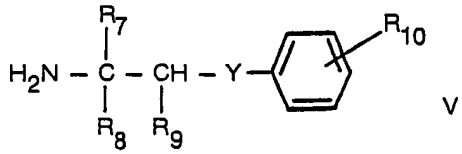
I_6

wherein R_1, R_2, R_3, R_4, R_7, R_8, R_9, R_{10} and Y have the same significance as in formula I can be produced by condensing the compounds shown by the general formulae



IV

and



V

and then reducing the product thus obtained.

This reaction is performed by condensing the compounds of formulae IV and V in an organic solvent such as methanol, ethanol, toluene, acetonitrile, tetrahydrofuran, etc., and then reducing the product, e.g. in the presence of PtO_2 catalyst or Raney nickel catalyst or with $NaBH_4$, $LiAlH_4$, etc.

The isolation and purification of the compounds of this invention shown by general formulae I_1—I_6 and formed by Process 1 or 2 may be effected by filtration, extraction with a solvent, separation by column chromatography, recrystallization, etc.

The pharmacological effects of compounds of this invention were determined by the following experiments. The effects of compounds of this invention were compared with those of 5 - {1 - hydroxy - 2 - [2 - (2 - methoxyphenoxy)ethylamino]ethyl} - 2 - methylbenzenesulfonamide (Compound A, which is one of the typical compounds presented in British Patent No. 2,006,772) and of phentolamine.

A. α-Adrenergic blocking action:

The blood pressure was measured in rats anesthetized with urethane and treated with pentolinium. The effects of the test samples (intravenous injection — i.v.) on the hypertensive response to phenylephrine (10 μg/Kg i.v.) were measured and the results are shown in Table I.

B. Antihypertensive effects in spontaneously hypertensive rats:

Oral administration (p.o.): The systolic blood pressure of spontaneously hypertensive rats having systolic blood pressure higher than 150 mmHg was measured indirectly by the tail cuff method using a programmed electrosphygmanometer (Narco Bio-Systems Inc., PE—300), the results being shown in Table II.

TABLE I α-Adrenergic blocking action:

Sample Compounds of this invention (Ex. No.)	α-adrenergic blocking ED_{50} (mg/Kg) i.v. (effective mean dose)
4	0.00035
5	0.00026
10	0.0059
11	0.012
12	0.0073
15	0.0013
16	0.0008
20	0.00000014
25	0.0012
26	0.004
Known Compounds	
Compound A	0.034
Phentolamine	0.061

TABLE II Antihypertensive effect:

Sample Compounds of this invention Ex. No.)	Dose (mg/Kg)	Change in systolic blood pressure (mmHg) at stated dose p.o.
10	10	−57 ± 5.6
11	30	−50 ± 4.7
12	10	−48 ± 2.0
15	10	−54 ± 6.2
16	10	−71 ± 11.1
20	3	− 57 ± 4.2
25	10	−46 ± 3.6
26	10	−46 ± 4.3
Known compounds		
Compound A	10	−35 ± 6.4
Phentolamine	10	+7.8 ± 5.0
Phentolamine	100	−70 ± 10.1

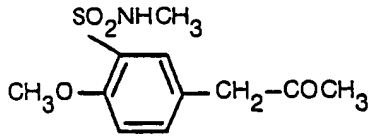
The clinical administration of the compounds of this invention is usually practiced by intravenous injection or orally as the free bases or the acid addition salts thereof (e.g. hydrochlorides, sulfates, maleates, acetates, fumarates, lactates, citrates, etc.). It is appropriate to administer 10 ng—1 mg doses of the compound several times per day in the case of intravenous administration, or 0.1—100 mg of the compound two or three times per day in the case of oral administration.

The compounds of this invention may be formulated into ordinary dosage forms such as, for example, tablets, capsules, pills, solutions, etc., and these medicaments can be prepared by conventional methods using usual medical excipients.

The production of compounds of this invention is illustrated in the following Examples.

In addition, the raw materials used in this invention include novel compounds and the production thereof is shown in Reference Examples.

Reference Example 1



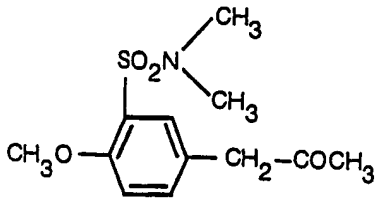
(1) To 250 g of chlorosulfonic acid was added dropwise 50 g of 4-methoxyphenylacetone at 0—5°C. After stirring the mixture for 4 hours at room temperature, the reaction mixture was poured into 2,500 ml of ice water and extracted thrice with 500 ml of ethyl acetate. The extract was washed with water and after drying the extract with anhydrous magnesium sulfate, the solvent was distilled off under reduced pressure. The crude crystals obtained were recrystallized from benzene-ether to provide 32 g of 3-chlorosulfonyl-4-methoxyphenylacetone.

Melting point: 80—81°C.

(2) In 26 ml of tetrahydrofuran was dissolved 2.6 g of 3-chlorosulfonyl-4-methoxyphenylacetone and then 1.2 g of 40% methylamine was added dropwise to the solution at a temperature lower than 10°C. After stirring the mixture for one hour at room temperature, the solvent was distilled off under reduced pressure and the residue was extracted with ethyl acetate. The extract was washed with water and after drying with anhydrous magnesium sulfate, the solvent was distilled off under reduced pressure. The crude crystals obtained were recrystallized from isopropanol-ether to provide 1.8 g of 4-methoxy-3-N-methylsulfamylphenylacetone.

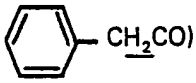
Melting point: 100—101°C.

Reference Example 2

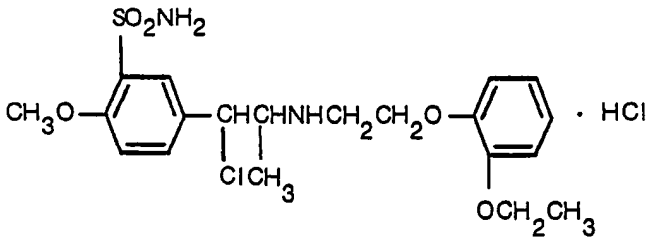


By reacting 2.6 g of 3-chlorosulfonyl-4-methoxyphenylacetone and 0.6 g of dimethylamine in the same manner as in Reference example 1—(2), 2.5 g of oily 4-methoxy-3-N,N-dimethylsulfamylphenylacetone was obtained.

Nuclear magnetic resonance spectra ($CDCl_3$):

δ: 2.18 (3H, S, $COCH_3$)
2.82 (6H, S, $N(CH_3)_2$)
3.69 (2H, S,  CH_2CO)
3.90 (3H, S, O—CH_3)

Example 1



In 1,000 ml of acetonitrile was suspended 17 g of 5 - [2 - [2 - (2 - ethoxyphenoxy)-ethylamino] - 1 - hydroxy - 2 - methylethyl] - 2 - methoxybenzenesulfonamide hydrochloride and while stirring the suspension, 9 g of thionyl chloride was added dropwise to the suspension at room temperature, whereby the product first dissolved and then began to crystallize gradually. After stirring the mixture for two days, the crystals formed were recovered by filtration, washed with chloroform and dried to provide 15 g of 5 - [1 - chloro - 2 - [2 - (2 - ethoxyphenoxy)ethylamino] - 2 - methylethyl] - 2 - methoxybenzenesulfonamide hydrochloride.

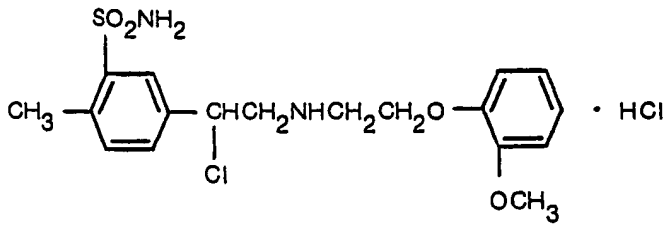
The product has the following physicochemical properties:
Melting point: 197—200°C
Elemental analysis for $C_{20}H_{27}N_2O_5SCl \cdot HCL$:

	C(%)	H(%)	N(%)
Calcd.:	50.11	5.89	5.84
Found:	50.06	5.96	5.95

Nuclear magnetic resonance spectra (CD_3OD):
δ 1.30 (3H, d, CH—CH_3)
1.40 (3H, t, CH_2—CH_3)
3.63 (2H, t, CH_2—CH_2—N)
4.01 (3H, s, O—CH_3)
4.12(2H, q, CH_3—CH_2—O)
4.36 (2H, t, CH_2—CH_2—O)
5.30 (1H, d, Cl—CH)

The compounds in Examples 2 and 3 were obtained in the same manner as in Example 1.

Example 2



5 - [1 - Chloro - 2 - [2 - (2 - methoxyphenoxy)ethylamino]ethyl] - 2 - methylbenzenesulfonamide hydrochloride

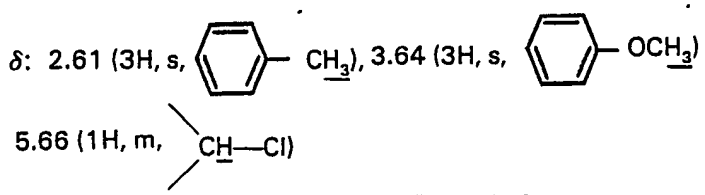
Physicochemical properties:

Melting point: 190—191°C

Elemental analysis for $C_{18}H_{23}N_2O_4SCl \cdot HCl$:

	C(%)	H(%)	N(%)
Calculated:	49.66	5.56	6.43
Found:	49.51	5.70	6.53

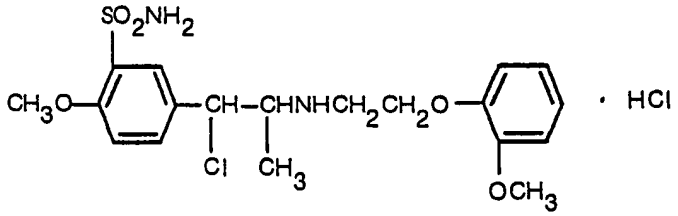
Nuclear magnetic resonance spectra (d_6-DMSO):



δ: 2.61 (3H, s, CH_3), 3.64 (3H, s, OCH_3)

5.66 (1H, m, CH—Cl)

Example 3



5 - [1 - Chloro - 2 - [2 - (2 - methoxyphenoxy)ethylamino] - 2 - methylethyl] - 2 - methoxybenzenesulfonamide hydrochloride

Physicochemical properties:

Melting point: 195—197°C (decomposed)

Elemental analysis for $C_{19}H_{25}N_2O_5SCl \cdot HCl$:

	C(%)	H(%)	N(%)
Calculated:	49.04	5.63	6.02
Found:	49.02	5.64	6.08

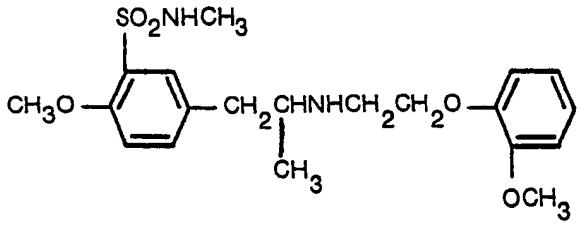
Nuclear magnetic resonance spectra (CD_3OD + d_6-DMSO):

δ: 1.18 (3H, d, CH—CH_3)

3.80 and 3.95 (3H + 3H, s, —O—CH_3)

5.56 (1H, d, CH—Cl)

Example 4



A mixture of 1.4 g of 4-methoxy-3-N-methylsulfamylphenylacetone, 1 g of 2-methoxyphenoxyethylamine, and 30 ml of methanol was refluxed for one hour. After cooling the mixture, 60 mg of a platinum oxide catalyst was added thereto, and reduction was performed at normal temperature and pressure. After absorption of a theoretical amount of hydrogen, the catalyst was filtered away. After the filtrate was acidified with alcoholic 5% hydrochloric acid, the solvent was distilled off under reduced pressure to form 1.6 g of crystals, which were recovered and recrystallized to provide 1.2 g of the colorless crystals of 2-methoxy-5-[2-[2-(2-methoxyphenoxy)ethylamino]-2-methylethyl]-N-methylbenzenesulfonamide hydrochloride.

The product has the following physicochemical properties:

Melting point: 162—163°C.

Elemental analysis for $C_{20}H_{28}N_2O_5S.HCl$:

	C(%)	H(%)	N(%)
Calcd.:	53.99	6.57	6.30
Found:	53.85	6.70	6.27

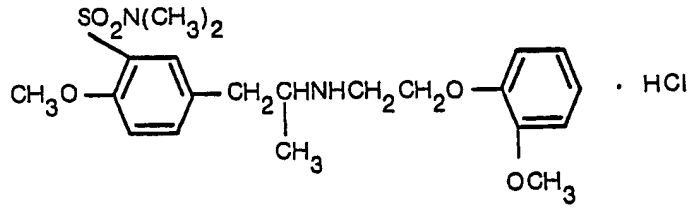
Nuclear magnetic resonance spectra (d_6-DMSO):

δ: 1.15 (3H, d, —$CHCH_3$)

3.76 and 3.88 (3H + 3H, S, O—CH_3)

The compound of Example 5 was obtained in the same manner as in Example 4.

Example 5



2 - Methoxy - 5 - [2 - [2 - (2 - methoxyphenoxy)ethylamino] - 2 - methylethyl] - N,N - dimethylbenzenesulfonamide hydrochloride

Physicochemical properties:

Melting point: 185—187°C.

Elemental analysis for $C_{21}H_{30}N_2O_5S{\cdot}HCl$:

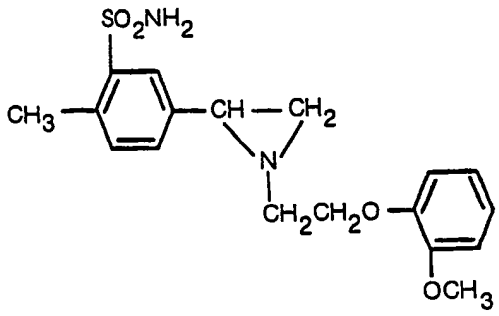
	C(%)	H(%)	N(%)
Calcd.:	54.95	6.81	6.10
Found:	54.73	6.88	5.85

Nuclear magnetic resonance spectra (d_6-DMSO):

δ: 1.16 (3H, d, $CHCH_3$). 2.71 (6H, s, $N(CH_3)_2$)

3.76 and 3.87 (3H + 3H, s, —O—CH_3)

Reference example 3



In 50 ml of ethyl acetate was suspended 4.35 g (0.01 mole) of 5-{1-chloro-2-[2-(2-methoxyphenoxy)ethylamino]ethyl}-2-methylbenzenesulfonamide hydrochloride and then 50 ml of an aqueous 10% sodium carbonate solution was added to the suspension with stirring. After further stirring overnight vigorously, the reaction mixture was recovered by decantation. After removing inorganic matter by passing the ethyl acetate layer thus recovered through a silica gel column (50 ml of silica gel), the reaction product was evaporated to dryness to provide 3.2 g (88%) of colorless resinous 5-[1-[2-(2-methoxyphenoxy)ethyl]aziridin-2-yl}-2-methylbenzenesulfonamide.

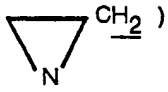
The product has the following physicochemical properties:

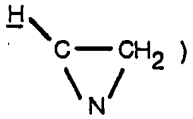
Amorphous form.

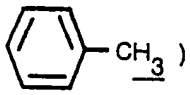
Elemental analysis for $C_{18}H_{22}N_2O_4S$:

	C(%)	H(%)	N(%)
Calcd.:	59.65	6.12	7.73
Found:	59.37	6.12	7.61

Nuclear magnetic resonance spectra ($CDCl_3$):

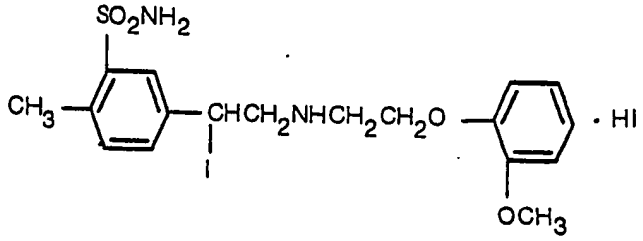
δ: 1.74 and 1.95 (1H + 1H, d, )

2.43 (1H, q, )

2.55 (3H, s )

4.10 (2H, t, O—CH_2—)

Example 6

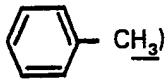


In 50 ml of dioxane was dissolved 2.5 g of 5-[1-[2-(2-methoxyphenoxy)ethyl]aziridin-2-yl}-2-methylbenzenesulfonamide and after adding thereto 1 g of concentrated hydroiodic acid, the mixture was stirred overnight. After the reaction was over, the solvent was distilled off under reduced pressure and the residue was washed thrice with 30 ml of water and then thrice with 200 ml of ether and crystallized by the addition of ethyl acetate. The crystals were recovered by filtration, washed with water, and dried to provide 1.7 g of 5-[-1-iodo-2-[2-(2-methoxyphenoxy)ethylamino]ethyl}-2-methylbenzenesulfonamide hydroiodide.

The product has the following physicochemical properties:
Melting point: 154—155°C.
Elemental analysis for $C_{18}H_{23}N_2O_4SI.HI$:

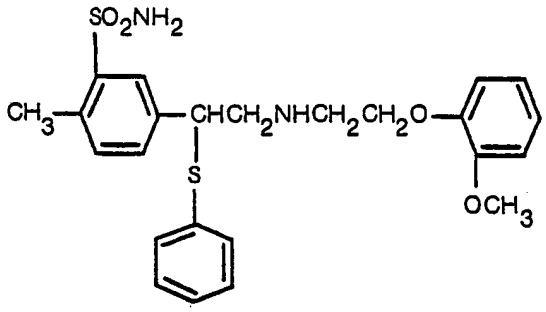
	C(%)	H(%)	N(%)
Calcd.:	34.97	3.91	4.53
Found:	35.07	3.98	4.39

Nuclear magnetic resonance spectra (CD_3OD):

δ: 2.65 (3H, s, )

3.54 (2H, t, —CH_2—N—)
4.30 (2H, t, —CH_2—O)
5.55 (1H, t, >CH—I)

Example 7

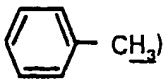


In 50 ml of methanol was dissolved 2.5 g of 5-{-1-[2-(2-methoxyphenoxy)ethyl]aziridin-2-yl}-2-methylbenzenesulfonamide and after adding 1 g of thiophenol to the solution and stirring the mixture overnight at room temperature, methanol was distilled off. The residue was subjected to silica gel column chromatography and the product was eluted by a mixed solvent of chloroform and methanol (9:1 by volume ratio) to provide 2.4 g of 5-{2-[2-(2-methoxyphenoxy)ethylamino]-1-phenylthioethyl}-2-methylbenzenesulfonamide as a viscous oily material.

The product has the following physicochemical properties:
Amorphous form.
Elemental analysis for $C_{24}H_{28}N_2O_4S_2$:

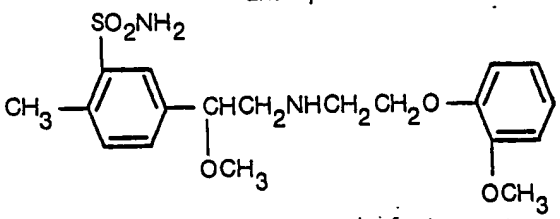
	C(%)	H(%)	N(%)
Calcd.:	60.99	5.97	5.93
Found:	60.72	6.11	5.71

Nuclear magnetic resonance spectra ($CDCl_3$):

δ: 2.58 (3H, s, )

3.74 (3H, s, O—CH_3)
3.98 (2H, t, —CH_2—O)
4.35 (1H, t, >CH—S)

Example 8



In 50 ml of methanol was dissolved 2.5 g of 5-{1-[2-(2-methoxyphenoxy)ethyl]aziridin-2-yl}-2-

methylbenzenesulfonamide and after adding thereto 2 ml of a boron trifluoride ether complex at room temperature, the mixture was stirred overnight. Thereafter, methanol was distilled off under reduced pressure and the residue was subjected to silica gel column chromatography and eluted with a mixed solvent of chloroform and methanol (9:1 by volume ratio), whereby 1.5 g of a colorless viscous oily material was obtained. The product was crystallized by the addition of 5 ml of methanol and several drops of ammonia. The crystals formed were recovered by filtration, washed with water, and dried to provide 1.2 g of 5-[1-methoxy-2-[2-(2-methoxyphenoxy)ethylamino]ethyl]-2-methylbenzenesulfonamide.

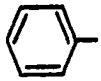
The product has the following physicochemical properties:

Melting point: 150—152°C.

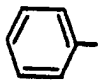
Elemental analysis for $C_{19}H_{26}N_2O_5S$:

	C(%)	H(%)	N(%)
Calcd.:	57.85	6.64	7.10
Found:	57.58	6.79	7.24

Nuclear magnetic resonance spectra (CD_3OD):

δ: 2.65 (3H, s,  CH_3)

2.98 (2H, t, $-CH_2N$)

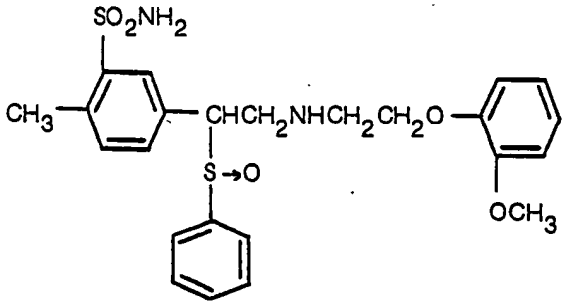
3.80 (3H, s,  OCH_3)

3.26 (3H, s, $CH-OCH_3$)

4.10 (2H, t, $-CH_2O$)

4.40 (1H, q, $>CH-O$)

Example 9



In 20 ml of acetic acid was dissolved 2 g of 5-[2-[2-(2-methoxyphenoxy)ethylamino]-1-phenylthioethyl]-2-methylbenzenesulfonamide and after adding thereto 0.5 ml of 30% H_2O_2, the mixture was heated to 50—60°C for 3 hours. After adding thereto 100 ml of water, the reaction mixture was extracted with 200 ml of ethyl acetate. The ethyl acetate extract was washed with an aqueous 1% sodium carbonate solution and then ethyl acetate was distilled off under reduced pressure. The residue was subjected to silica gel column chromatography, the product was eluted with a mixed solvent of chloroform and methanol (9:1 by volume ratio), and the colorless viscous oily product thus obtained was crystallized by the addition of ethyl acetate. The crystals formed were recovered by filtration to provide 1.3 g of 5-[2-[2-(2-methoxyphenoxy)ethylamino]-1-phenylsulfinylethyl]-2-methylbenzenesulfonamide.

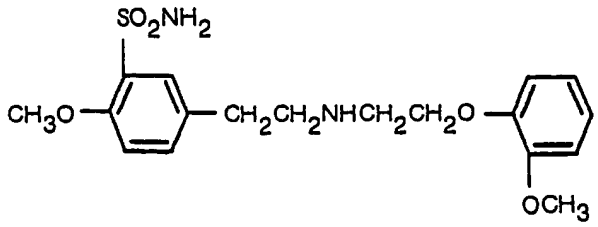
The product has the following physicochemical properties:

Melting point: 139—141°C

Elemental analysis for $C_{24}H_{28}N_2O_5S_2$:

	C(%)	H(%)	N(%)
Calcd.:	59.00	5.78	5.73
Found:	58.91	5.74	5.72

Example 10



In 150 ml of methanol was dissolved 3.8 g of 5-[1-chloro-2-[2-(2-methoxyphenoxy)ethylamino]ethyl]-2-methoxybenzenesulfonamide hydrochloride and after adding thereto 0.5 g of 10% palladium carbon, dechlorination was performed under hydrogen stream at normal temperature and pressure. The palladium carbon was filtered away and the filtrate was concentrated under reduced pressure to provide 3.1 g of 2-methoxy-5-[2-[2-(2-methoxyphenoxy)ethylamino]ethyl] benzenesulfonamide hydrochloride, which was recrystallised from 120 ml of a mixture of methanol and ethanol (1:4 by volume ratio) to provide 2.3 g of the colorless crystals thereof.

The product has the following physicochemical properties:

Melting point: 196—198°C

Elemental analysis for $C_{18}H_{24}N_2O_5S.HCl$:

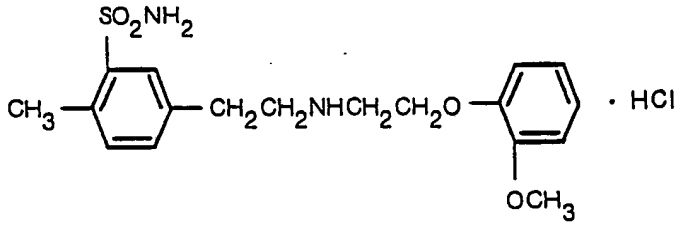
	C(%)	H(%)	N(%)
Calcd.:	51.86	6.04	6.72
Found:	51.72	6.23	6.68

Nuclear magnetic resonance spectra (CD_3OD):

δ: 3.84 and 3.98 (3H + 3H, s, —OCH_3)
4.24 (2H, t, —OCH_2—)

The compounds in Examples 11—29 were obtained in the same manner as in Example 10.

Example 11



5-[2-[2-(2-Methoxyphenoxy)ethylamino]ethyl]-2-methylbenzenesulfonamide hydrochloride.

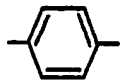
Physicochemical properties:

Melting point: 173—175°C

Elemental analysis for $C_{18}H_{24}N_2O_4S{\cdot}HCl$:

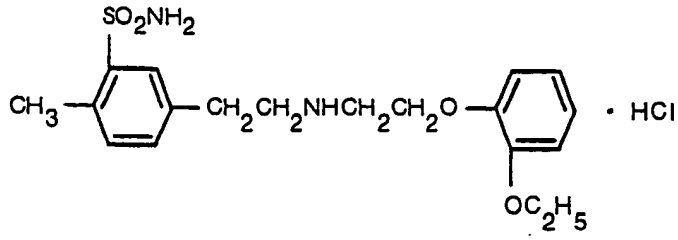
	C(%)	H(%)	N(%)
Calcd.:	53.93	6.28	6.99
Found:	53.83	6.27	6.97

Nuclear magnetic resonance spectra (CD_3OD):

δ: 2.64 (3H, s, CH_3 

3.84 (3H, s, —OCH_3)
4.28 (2H, t, —OCH_2—)

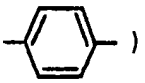
Example 12



5-[2-[2-(2-Ethoxyphenoxy)ethylamino]ethyl]-2-methylbenzenesulfonamide hydrochloride.
Physicochemical properties:
Melting point: 180—181.5°C
Elemental analysis for $C_{19}H_{26}N_2O_4S \cdot HCl$:

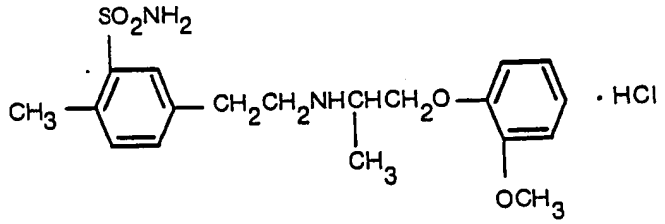
	C(%)	H(%)	N(%)
Calcd.:	55.00	6.56	6.75
Found:	54.81	6.56	6.89

Nuclear magnetic resonance spectra (CD_3OD):

δ: 1.36 (3H, t, $-OCH_2\underline{CH_3}$), 2.64 (3H, s, $\underline{CH_3}$ )

4.10 (2H, q, $-OCH_2\underline{CH_3}$), 4.36 (2H, t, $-OCH_2-CH_2-$)

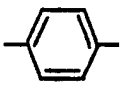
Example 13



5 - [2 - [2 - (2 - Methoxyphenoxy) - 1 - methylethylamino]ethyl] - 2 - methylbenzenesulfonamide hydrochloride.
Physicochemical properties:
Melting point: 169—171°C
Elemental analysis for $C_{19}H_{26}N_2O_4S \cdot HCl$:

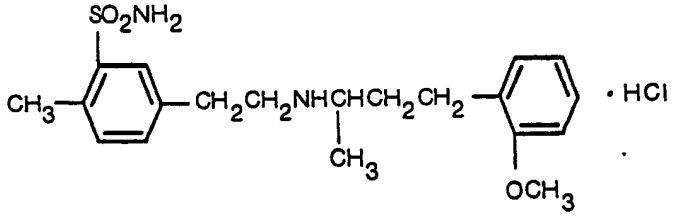
	C(%)	H(%)	N(%)
Calcd.:	55.00	6.56	6.75
Found:	54.89	6.60	6.76

Nuclear magnetic resonance spectra (CD_3OD):

δ: 1.15 (3H, d, $>CH-\underline{CH_3}$), 2.64 (3H, s, $\underline{CH_3}$ )

3.80 (3H, s, $-O\underline{CH_3}$)

Example 14



5 - {2 - [3 - (2 - Methoxyphenyl) - 1 - methylpropylamino]ethyl} - 2 - methylbenzenesulfonamide hydrochloride.

Physicochemical properties:

Melting point: 198—200°C

Elemental analysis for $C_{20}H_{28}N_2O_3S \cdot HCl$:

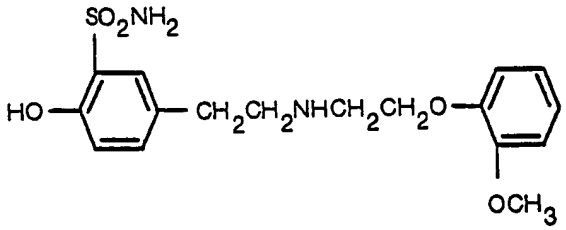
	C(%)	H(%)	N(%)
Calcd.:	58.17	7.08	6.78
Found:	58.09	7.01	6.62

Nuclear magnetic resonance spectra (d_6-DMSO):

δ: 1.35 (3H, d, >CH—CH_3), 2.55 (3H, s, CH_3—⟨⟩)

3.78 (3H, s, —OCH_3)

Example 15



2-Hydroxy-5-{2-[2-(2-methoxyphenoxy)ethylamino]ethyl}benzenesulfonamide.

Physicochemical properties:

Melting point: 97—99°C.

Elemental analysis for $C_{17}H_{22}N_2O_5S \cdot H_2O$:

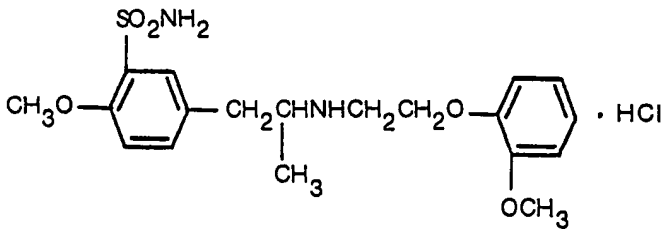
	C(%)	H(%)	N(%)
Calcd.:	53.10	6.29	7.29
Found:	52.75	6.22	7.09

Nuclear magnetic resonance spectra (d_6-DMSO):

δ: 3.76 (3H, s, —OCH_3)

4.04 (2H, t, —OCH_2—)

Example 16



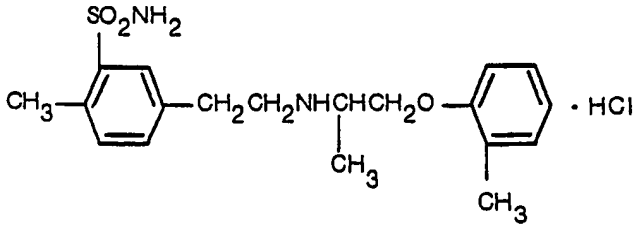
2 - Methoxy - 5 - {2 - [2 - (2 - methoxyphenoxy)ethylamino] - 2 - methylethyl}benzenesulfonamide hydrochloride.

Physicochemical properties:
Melting point: above 250°C
Elemental analysis for $C_{19}H_{26}N_2O_5S \cdot HCl$:

	C(%)	H(%)	N(%)
Calcd.:	52.96	6.31	6.50
Found:	52.44	6.31	6.47

Nuclear magnetic resonance spectra (d_6-DMSO):
δ: 1.15 (3H, d, >CH—CH_3)
3.78 and 3.90 (3H + 3H, s, —OCH_3)
4.38 (2H, t, —OCH_2—)

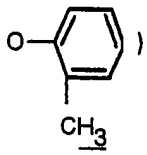
Example 17

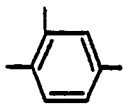


2 - Methyl - 5 - [2 - [2 - (2 - methylphenoxy) - 1 - methylethylamino]ethyl]benzenesulfonamide hydrochloride.
Physicochemical properties:
Melting point: 183—185°C
Elemental analysis for $C_{19}H_{26}N_2O_3S \cdot HCl$:

	C(%)	H(%)	N(%)
Calcd.:	57.20	6.82	7.02
Found:	57.13	6.79	6.99

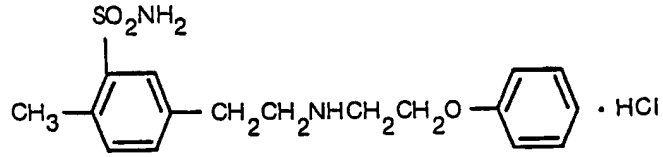
Nuclear magnetic resonance spectra (CD_3OD):

δ: 1.55 (3H, d, >CH—CH_3) 2.24 (3H, s, )

2.64 (3H, s, CH_3  C)

2.08—2.40 (2H, m, —OCH_2—)

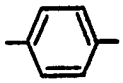
Example 18



2-Methyl-5-[2-(2-phenoxyethylamino)ethyl]benzenesulfonamide hydrochloride.
Physicochemical properties:
Melting point: 208.5—210°C
Elemental analysis for $C_{17}H_{22}N_2O_3S \cdot HCl$:

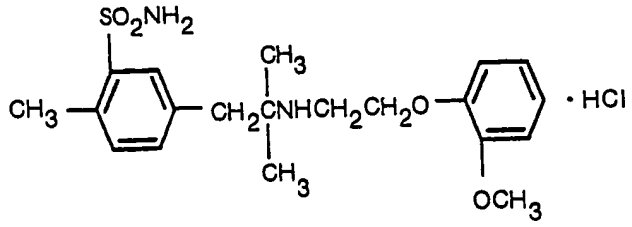
	C(%)	H(%)	N(%)
Calcd.:	55.05	6.25	7.55
Found:	54.83	6.23	7.48

Nuclear magnetic resonance spectra: (CD_3OD):

δ: 2.65 (3H, s, $\underline{CH_3}$— )

4.32 (2H, t, —$OCH_{\underline{2}}$—)

Example 19



5 - {2 - [2 - (2 - Methoxyphenoxy)ethylamino] - 2,2 - dimethylethyl} - 2 - methylbenzenesulfonamide hydrochloride

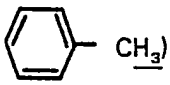
Physicochemical properties:

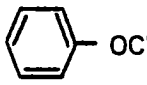
Melting point: 199—202°C

Elemental analysis for $C_{20}H_{28}N_2O_4S \cdot HCl \cdot CH_3OH$:

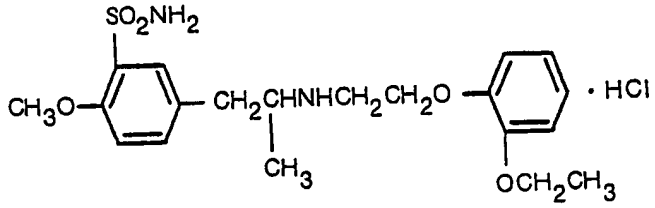
	C(%)	H(%)	N(%)
Calcd.:	54.71	7.21	6.08
Found:	54.50	7.17	6.14

Nuclear magnetic resonance spectra (d_6—DMSO):

δ: 1,24 (6H, s, —$\underset{|}{\overset{|}{C}}$—$\underline{CH_3}$), 2.56 (3H, s,  —$\underline{CH_3}$)

3.74 (3H, s,  —$O\underline{CH_3}$),4.30 (2H, t, —$\underline{CH_2}$—O)

Example 20



5 - {2 - [2 - (2 - Ethoxyphenoxy)ethylamino] - 2- methylethyl} - 2 - methoxybenzenesulfonamide hydrochloride.

Physicochemical properties:

Melting point: 254—256°C

Elemental analysis for $C_{20}H_{28}N_2O_5S \cdot HCl$:

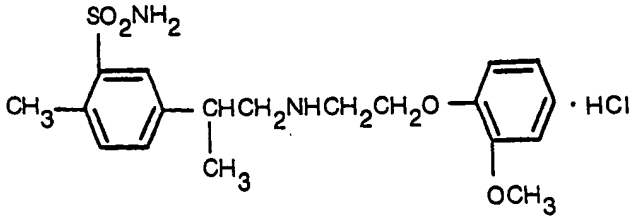
	C(%)	H(%)	N(%)
Calcd.:	53.99	6.57	6.30
Found:	53.79	6.58	6.26

Nuclear magnetic resonance spectra (CD_3OD):

δ: 1.28 (3H, d, >CH—$\underline{CH_3}$), 1.38 (3H, t, $CH_2\underline{CH_3}$)

3.97 (3H, s, O—$\underline{CH_3}$), 4.30 (2H, t, CH_2—$\underline{CH_2}$—O)

Example 21



5 - [2 - [2 - (2 - Methoxyphenoxy)ethylamino] - 1 - methylethyl] - 2 - methylbenzenesulfonamide hydrochloride.

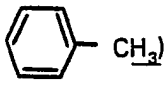
Physicochemical properties:

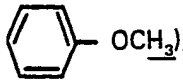
Melting point: 183—185°C

Elemental analysis for $C_{19}H_{26}N_2O_4S \cdot HCl$:

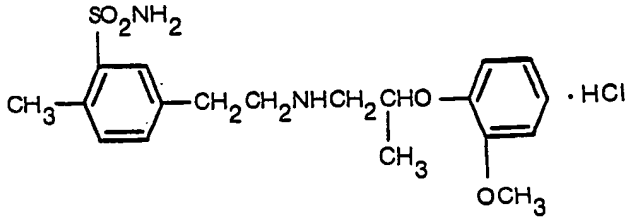
	C(%)	H(%)	N(%)
Calcd.:	55.00	6.56	6.75
Found:	54.76	6.56	6.74

Nuclear magnetic resonance spectra (CD_3OD):

δ: 1.40 (3H, d, >CH—$\underline{CH_3}$), 2.64 (3H, s, )

3.80 (3H, s, ), 4.23 (2H, t, —$\underline{CH_2}$—O)

Example 22



5 - [2 - [2 - (2 - Methoxyphenoxy) - 2 - methylethylamino]ethyl] - 2 - methylbenzenesulfonamide hydrochloride.

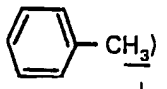
Physicochemical properties:

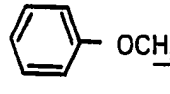
Melting point: 231—232°C.

Elemental analysis for $C_{19}H_{26}N_2O_4S \cdot HCl$:

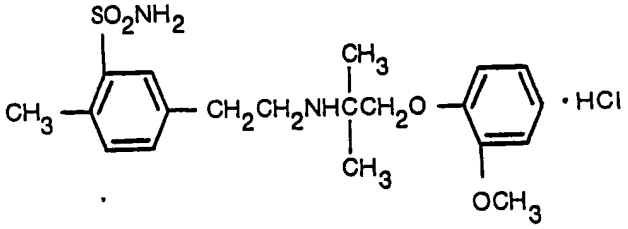
	C(%)	H(%)	N(%)
Calcd.	55.00	6.56	6.75
Found:	54.86	6.58	6.83

Nuclear magnetic resonance spectra (CD_3OD):

δ: 1.26 (3H, d, >CH—$\underline{CH_3}$), 2.60 (3H, s, )

3.76 (3H, s, ), 4.42 (1H, m, CH_3—$\underline{CH}$—O)

Example 23



5 - [2 - [2 - (2 - Methoxyphenoxy) - 1,1 - dimethylethylamino]ethyl] - 2 - methylbenzenesulfonamide hydrochloride.

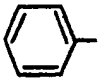
Physicochemical properties:

Melting point: 191—193°C

Elemental analysis for $C_{20}H_{28}N_2O_4S \cdot HCl$:

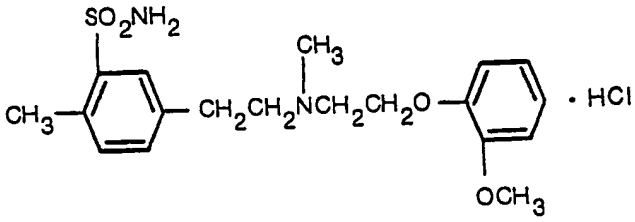
	C(%)	H(%)	N(%)
Calcd.:	56.00	6.81	6.53
Found:	55.83	6.86	6.32

Nuclear magnetic resonance spectra (d_6—DMSO):

δ: 1.44 (6H, s, N—C($\underline{CH_3}$)$_2$—C), 2.56 (3H, s,  $\underline{CH_3}$)

3.66 (3H, s,  $\underline{OCH_3}$), 4.08 (2H, s, —$\underline{CH_2}$—O)

Example 24



5 - [2 - [N - [2 - (2 - Methoxyphenoxyl)ethyl] - N - methylamino]ethyl] - 2 - methylbenzenesulfonamide hydrochloride.

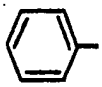
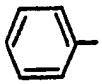
Physicochemical properties:

Melting point: 169—171°C

Elemental analysis for $C_{19}H_{26}N_2O_4S \cdot HCl$:

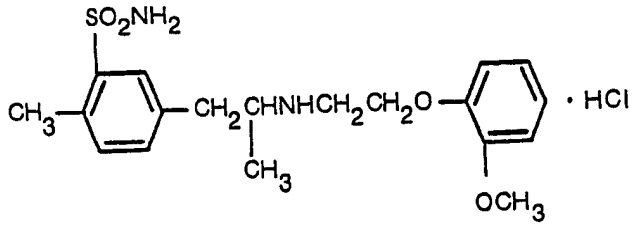
	C(%)	H(%)	N(%)
Calcd.	55.00	6.56	6.75
Found:	54.88	6.51	6.64

Nuclear magnetic resonance spectra (d_6—DMSO):

δ: 2.56 (3H, s,  $\underline{CH_3}$), 3.68, (3H, s,  —$\underline{OCH_3}$)

4.39 (2H, t, —$\underline{CH_2}$—O)

Example 25



5 - {2 - [2 - (2 - Methoxyphenoxy)ethylamino] - 2 - methylethyl} - 2 - methylbenzenesulfonamide hydrochloride.

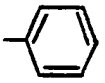
Physicochemical properties:

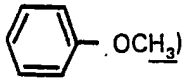
Melting point: 250—252°C

Elemental analysis for $C_{19}H_{26}N_2O_4S \cdot HCl$:

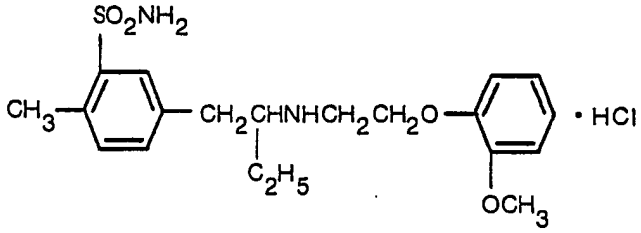
	C(%)	H(%)	N(%)
Calcd.:	55.00	6.56	6.75
Found:	54.68	6.49	6.58

Nuclear magnetic resonance spectra ($CDCl_3$ + d_6-DMSO + D_2O + Na_2CO_3):

δ: 1.06 (3H, d, $>CHCH_3$), 2.61 (3H, s, CH_3 )

3.76 (3H, s, )

Example 26



5 - {2 - [2 - (2 - Methoxyphenoxy)ethylamino] - 2 - ethylethyl} - 2 - methylbenzenesulfonamide hydrochloride.

Physicochemical properties:

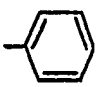
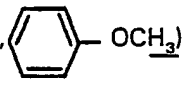
Melting point: 198—200°C

Elemental analysis for $C_{20}H_{28}N_2O_4S \cdot HCl$:

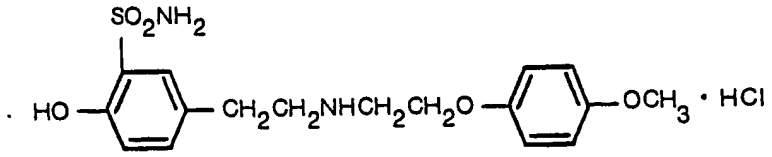
	C(%)	H(%)	N(%)
Calcd.:	56.00	6.81	6.53
Found:	55.76	6.88	6.51

Nuclear magnetic resonance spectra ($CDCl_3$ + d_6-DMSO + D_2O + Na_2CO_3):

δ: 0.94 (3H, t, $>CHCH_2CH_3$), 1.22 (2H, m, $>CHCH_2CH_3$)

2.56 (3H, s, CH_3 ), 3.76 (3H, s, )

Example 27



2 - Hydroxy - 5 - [2 - [2 - (4 - methoxyphenoxy)ethylamino]ethyl]benzenesulfonamide hydrochloride.

Physicochemical properties:

Melting point: 237—241°C (decomposed).

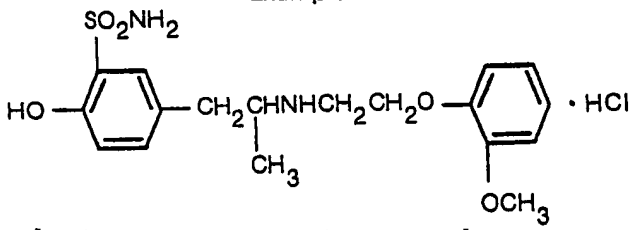
Elemental analysis for $C_{17}H_{22}N_2O_5S \cdot HCl$:

	C(%)	H(%)	N(%)
Calcd.:	50.68	5.75	6.95
Found:	50.45	5.64	6.99

Nuclear magnetic resonance spectra (CD_3OD):

δ: 3.74 (3H, s, O—CH_3), 4.22 (2H, t, —CH_2—O)

Example 28



2 - Hydroxy - 5 - [2 - [2 - (2 - methoxyphenoxy)ethylamino] - 2 - methylethyl]benzenesulfonamide hydrochloride.

Physicochemical properties:

Melting point: 211—214°C

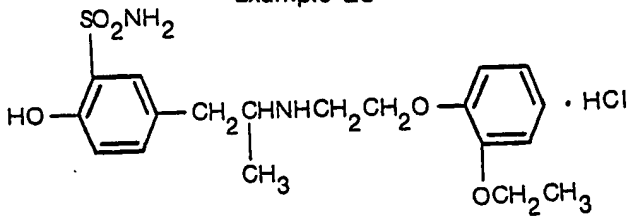
Elemental analysis for $C_{18}H_{24}N_2O_5S \cdot HCl$:

	C(%)	H(%)	N(%)
Calcd.:	51.86	6.04	6.72
Found:	51.72	6.00	6.59

Nuclear magnetic resonance (CD_3OD):

δ: 1.28 (3H, d, >CHCH_3), 3.86 (3H, s, —OCH_3)
4.30 (2H, t, —CH_2—O)

Example 29



5 - [2 - [2 - (2 - Ethoxyphenoxy)ethylamino] - 2 - methylethyl] - 2 - hydroxybenzenesulfonamide hydrochloride.

Physicochemical properties:

Melting point: 172—173°C

Elemental analysis for $C_{19}H_{26}N_2O_5S.HCl$:

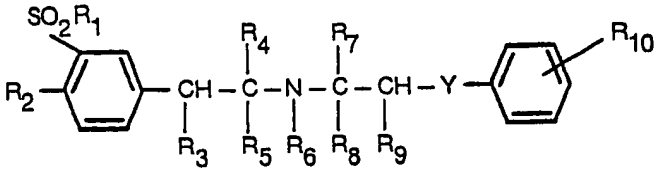
	C(%)	H(%)	N(%)
Calcd.:	52.96	6.31	6.50
Found:	52.83	6.65	6.12

Nuclear magnetic resonance spectra (CD_3OD):

1.26 (3H, d, >CHCH_3), 1.36 (3H, t, —CH_2CH_3)
4.10 (2H, q, —CH_2CH_3), 4.26 (2H, t, —CH_2CH_2—O)

Claims for the contracting states BE CH DE FR GB IT LI LU NL SE

1. A sulfamoylphenethylamine derivative represented by the general formula



wherein R_1 represents an amino group or a mono- or di-lower alkylamino group; R_2 represents a hydroxyl group, a lower alkyl group, or a lower alkoxy group; R_3 represents hydrogen, halogen, a lower alkyl group, a lower alkoxy group, a phenylthio group, or a phenylsulfinyl group; R_4, R_5, R_6, R_7, R_8, and R_9 are selected independently from hydrogen and lower alkyl groups; R_{10} represents hydrogen, a lower alkyl group, or a lower alkoxy group; and Y represents oxygen or a methylene group with the provisos that Y is oxygen when R_2 is a hydroxyl group, and R_1 is NH_2, R_2 is a lower alkyl group, R_3, R_4, R_5, R_6, R_7 and R_9 are hydrogen, R_8 is a lower alkyl group and R_{10} a lower alkoxy group when Y is a methylene group; or a salt thereof.

2. A compound according to claim 1 wherein R_3 is hydrogen or a lower alkyl group.

3. 5 - {2 - [2 - (2 - ethoxyphenoxy)ethylamino] - 2 - methylethyl} - 2 - methoxybenzenesulfonamide.

4. 2 - methoxy - 5 - {2 - [2 - (2 - methoxyphenoxy)ethylamino] - 2 - methylethyl}benzenesulfonamide.

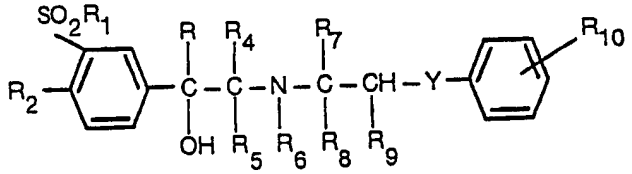
5. 5-{2-[2-(2-methoxyphenoxy)ethylamino]-2-methylethyl}-2-methylbenzenesulfonamide.

6. 5 - {2 - [2 - (2 - methoxyphenoxy)ethylamino]ethyl} - 2 - methylbenzenesulfonamide or 2-methoxy - 5 - {2 - [2 - (2 - methoxyphenoxy)ethylamino] - 2 - methylethyl} - N - methylbenzenesulfonamide or 2 - methoxy - 5 -{2 - [2 - (2 - methoxyphenoxy)ethylamino] - 2 - methylethyl} - N,N - dimethylbenzenesulfonamide.

7. A salt of a compound according to any of claims 3 to 6.

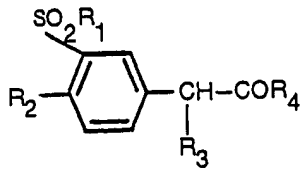
8. A pharmaceutical composition containing a compound according to any preceding claim and an excipient.

9. A process of producing a compound according to claim 1 which comprises reacting a compound represented by the general formula

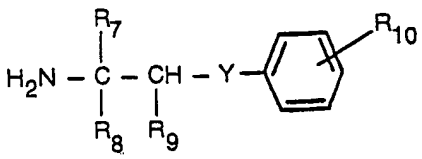


wherein R represents hydrogen or a lower alkyl group and R_1, R_2, R_4, R_5, R_6, R_7, R_8, R_9, R_{10}, and Y are as defined in claim 1 with halogenating agent and then, if desired, a) reducing the halogenated product; or b) reacting the halogenated product with a lower alcohol or thiophenol and, if desired, oxidizing the product obtained by the reaction with thiophenol; or c) reacting the halogenated product with alkaline material and then reacting the product thus obtained with hydrogen iodide, a lower alcohol, or thiophenol, and if desired, oxidizing the product obtained by the reaction with thiophenol.

10. A process of producing a compound according to claim 1, wherein R_5 and R_6 are hydrogen, which comprises condensing a compound represented by the general formula



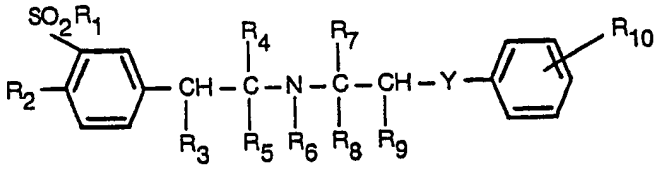
with a compound represented by the general formula



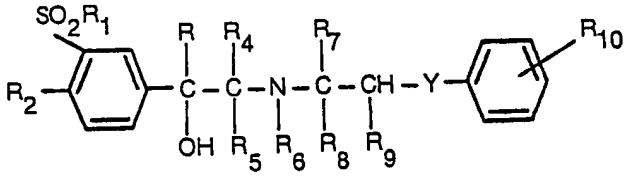
wherein R_1, R_2, R_3, R_4, R_7, R_8, R_9, R_{10} and Y are as defined in claim 1 and then reducing the condensation product.

Claims for contracting State AT

1. A process for producing a novel sulfamoylphenethylamine derivative represented by the general formula

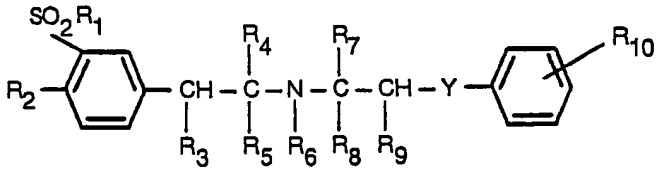


wherein R_1 represents an amino group or a mono- or di-lower alkylamino group; R_2 represents a hydroxyl group, a lower alkyl group, or a lower alkoxy group; R_3 represents hydrogen, halogen, a lower alkyl group, a lower alkoxy group, a phenylthio group, or a phenylsulfinyl group; R_4, R_5, R_6, R_7, R_8, and R_9 are selected independently from hydrogen and lower alkyl groups; R_{10} represents hydrogen, a lower alkyl group, or a lower alkoxy group; and Y represents oxygen or a methylene group with the provisos that Y is oxygen when R_2 is a hydroxyl group, and R_1 is NH_2, R_2 is a lower alkyl group, R_3, R_4, R_5, R_6, R_7 and R_9 are hydrogen, R_8 is a lower alkyl group and R_{10} a lower alkoxy group when Y is a methylene group; which process comprises reacting a compound represented by the general formula

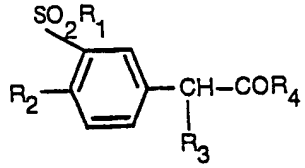


wherein R represents hydrogen or a lower alkyl group and R_1, R_2, R_4, R_5, R_6, R_7, R_8, R_9, R_{10} and Y are as defined above with halogenating agent and then, if desired, a) reducing the halogenated product; or b) reacting the halogenated product with a lower alcohol or thiophenol and, if desired, oxidizing the product obtained by the reaction with thiophenol; or c) reacting the halogenated product with alkaline material and then reacting the product thus obtained with hydrogen iodide, a lower alcohol, or thiophenol, and if desired, oxidizing the product obtained by the reaction with thiophenol.

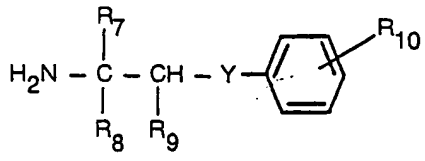
2. A process for producing a novel sulfamoylphenethylamine derivative represented by the general formula



wherein R_1 represents an amino group or a mono- or di-lower alkylamino group; R_2 represents a hydroxyl group, a lower alkyl group, or a lower alkoxy group; R_3 represents hydrogen, halogen, a lower alkyl group, a lower alkoxy group, a phenylthio group, or a phenylsulfinyl group; R_5 and R_6 are hydrogen; R_4, R_7, R_8, and R_9 are selected independently from hydrogen and lower alkyl groups; R_{10} represents hydrogen, a lower alkyl group, or a lower alkoxy group; and Y represents oxygen or a methylene group with the provisos that Y is oxygen when R_2 is a hydroxyl group, and R_1 is NH_2, R_2 is a lower alkyl group, R_3, R_4, R_7 and R_9 are hydrogen, R_8 is a lower alkyl group and R_{10} a lower alkoxy group when Y is methylene group; which process comprises condensing a compound represented by the general formula



with a compound represented by the general formula



wherein R_1, R_2, R_3, R_4, R_7, R_8, R_9, R_{10} and Y are as defined above and then reducing the condensation product.

3. A process according to claim 1 wherein R_3 is hydrogen or a lower alkyl group.

4. A process according to claim 1 for producing 5-{2-[2-(2-ethoxyphenoxy)ethylamino]-2-methylethyl}-2-methoxybenzenesulfonamide which process comprises reacting 5-{2-[2-(2-ethoxyphenoxy)-ethylamino]-1-hydroxy-2-methylethyl}-2-methoxybenzenesulfonamide hydrochloride with halogenating agent thionyl chloride.

5. A process according to claim 1 for producing 2-methoxy-5-{2-[2-(2-methoxyphenoxy)ethylamino]-2-methylethyl}benzenesulfonamide which process comprises reacting 2-methoxy-5-{2-[2-(2-methoxyphenoxy)ethylamino]-1-hydroxy-2-methylethyl}benzenesulfonamide with halogenating agent thionyl chloride.

6. A process according to claim 1 for producing 5-{2-[2-(2-methoxyphenoxy)ethylamino]-2-methylethyl}-2-methylbenzenesulfonamide which process comprises reacting 5-{2-[2-(2-methoxyphenoxy)ethylamino]-1-hydroxy-2-methylethyl}-2-methylbenzenesulfonamide with halogenating agent and reducing the halogenated product under hydrogen using a palladium carbon catalyst.

7. A process according to claim 1 for producing 5-{2-[2-(2-methoxyphenoxy)ethylamino]ethyl}-2-methylbenzenesulfonamide which process comprises reacting 5-{2-[2-(2-methoxyphenoxy)ethylamino]-1-hydroxy-2-ethyl}-2-methylbenzenesulfonamide with halogenating agent thionyl chloride.

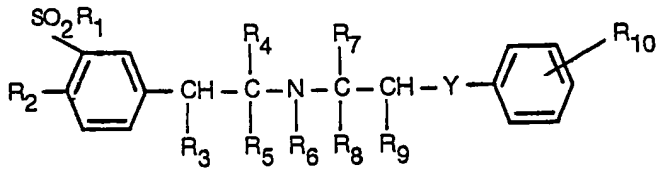
8. A process according to claim 2 for producing 2-methoxy-5-{2-[2-(2-methoxyphenoxy)ethylamino]-2-methylethyl}-N-methylbenzenesulfonamide which process comprises condensing 4-methoxy-3-N-methylsulfamylphenyl acetone with 2-methoxyphenoxyethylamine.

9. A process according to claim 2 for producing 2-methoxy-5-{2-[2-(2-methoxyphenoxy)ethylamino]-2-methylethyl}-N,N-dimethylbenzenesulfonamide which process condensing 4-methoxy-3-N,N-dimethylsulfamylphenyl acetone with 2-methoxyphenoxyethylamine.

10. A process according to any preceding claim which includes an additional step of converting the reaction product to salt form.

Patentansprüche fur die Vertragsstaaten: BE CH DE FR GB IT LI LU NL SE

1. Ein Sulfamoylphenäthylaminderivat, das durch die allgemeine Formel



wiedergegeben ist, worin R_1 eine Aminogruppe oder eine mono- oder di-niedrig-Alkylaminogruppe bedeutet; R_2 bedeutet eine Hydroxylgruppe, eine niedrige Alkylgruppe oder eine niedrige Alkoxygruppe; R_3 bedeutet Wasserstoff, Halogen, eine niedrige Alkylgruppe, eine niedrige Alkoxygruppe, eine Phenylthiogruppe oder eine Phenylsulfinylgruppe; R_4, R_5, R_6, R_7, R_8 und R_9 sind unabhängig voneinander aus Wasserstoff und niedrigen Alkylgruppen ausgewählt; R_{10} bedeutet Wasserstoff, eine niedrige Alkylgruppe oder eine Alkoxygruppe; und Y bedeutet Sauerstoff oder eine Methylengruppe mit den Maßgaben, daß Y Sauerstoff ist, wenn R_2 eine Hydroxylgruppe ist und R_1 NH_2 ist, R_2 ist eine niedrige Alkylgruppe, R_3, R_4, R_5, R_6, R_7 und R_9 sind Wasserstoff, R_8 ist eine niedrige Alkylgruppe und R_{10} eine niedrige Alkoxygruppe, wenn Y eine Methylengruppe ist; oder ein Salz desselben.

2. Eine Verbindung nach Anspruch 1, worin R_3 Wasserstoff oder eine niedrige Alkylgruppe ist.

3. 5-{2-[2-(2-Äthoxyphenoxy)äthylamino]-2-methyläthyl}-2-methoxybenzolsulfonamid.

4. 2-Methoxy-5-{2-[2-(2-methoxyphenoxy)äthylamino]-2-methyläthyl}benzolsulfonamid.

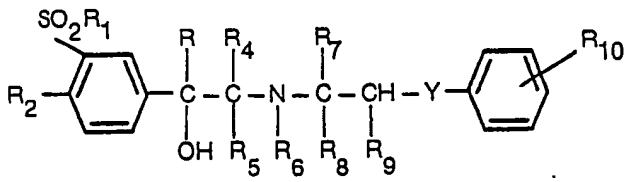
5. 5-{2-[2-(2-Methoxyphenoxy)äthylamino]-2-methyläthyl}-2-methylbenzolsulfonamid.

6. 5-{2-[2-(2-Methoxyphenoxy)-äthylamino]äthyl}-2-methylbenzolsulfonamid oder 2-Methoxy-5-{2-[2-(2-methoxyphenoxy)äthylamino]-2-methyläthyl}-N-methylbenzolsulfonamid oder 2-Methoxy-5-{2-[2-(2-methoxyphenoxy)äthylamino]-2-methyläthyl}-N,N-dimethylbenzolsulfonamid.

7. Ein Salz einer Verbindung nach einem der Ansprüche 3 bis 6.

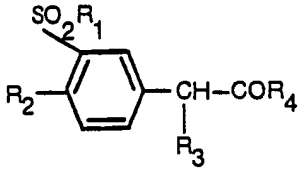
8. Eine pharmazeutische Zusammensetzung enthaltend eine Verbindung gemäß einem vorhergehenden Anspruch und ein Bindemittel.

9. Ein Verfahren zur Herstellung einer Verbindung nach Anspruch 1, gekennzeichnet durch das Umsetzen einer durch die allgemeine Formel

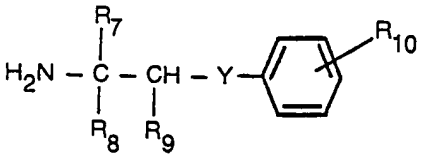


wiedergegebenen Verbindung, worin R Wasserstoff oder eine niedrige Alkylgruppe und R_1, R_2, R_4, R_5, R_6, R_7, R_8, R_9, R_{10} und Y so wie in Anspruch 1 definiert sind, mit einem Halogenierungsmittel und dann gewünschtenfalls a) durch Reduzieren des halogenierten Produktes oder b) Umsetzen des halogenierten Produktes mit einem niedrigen Alkohol oder Thiophenyl und, falls gewünscht, Oxidieren des durch die Reaktion mit Thiophenol erhaltenem Produktes oder c) Umsetzen des halogenierten Produktes mit einem alkalischen Stoff und nachfolgendem Umsetzen des so erhaltenen Produktes mit Jodwasserstoff, einem niedrigen Alkohol oder Thiophenol und, falls gewünscht, Oxidieren des durch die Reaktion mit Thiophenol erhaltenem Produktes.

10. Ein Verfahren zur Herstellung einer Verbindung nach Anspruch 1, worin R_5 und R_6 Wasserstoff sind, gekennzeichnet durch die Kondensation einer durch die allgemeine Formel



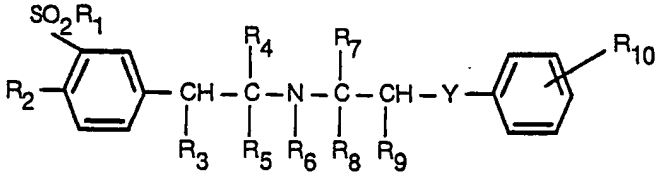
wiedergegebenen Verbindung mit einer Verbindung, welche durch die allgemeine Formel



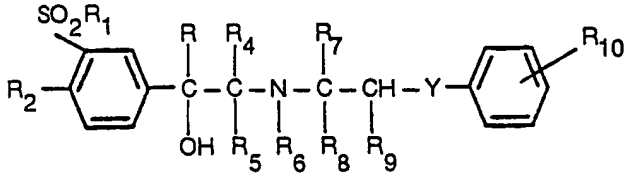
wiedergegeben ist, worin R_1, R_2, R_3, R_4, R_7, R_8, R_9, R_{10} und Y wie im Anspruch 1 definiert sind und durch nachfolgendes Reduzieren des Kondensationsproduktes.

Patentansprüche fur den Vertragsstaat: AT

1. Ein Verfahren zur Herstellung eines neuen Sulfamoylphenäthylaminderivates, das durch die allgemeine Formel

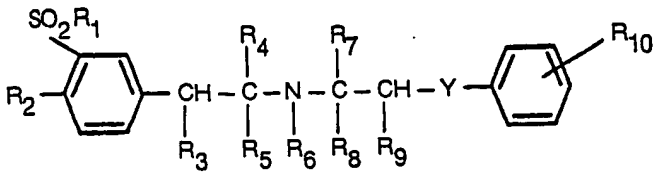


wiedergegeben ist, worin R_1 eine Aminogruppe oder eine mono- oder di-niedrig-Alkylaminogruppe bedeutet; R_2 bedeutet eine Hydroxylgruppe, eine niedrige Alkylgruppe oder eine niedrige Alkoxygruppe; R_3 bedeutet Wasserstoff, Halogen, eine niedrige Alkylgruppe, eine niedrige Alkoxygruppe, eine Phenylthiogruppe oder eine Phenysulfinylgruppe; R_4, R_5, R_6, R_7, R_8 und R_9 sind unabhängig voneinander unter Wasserstoff und niedrigen Alkylgruppen ausgewählt; R_{10} bedeutet Wasserstoff, eine niedrige Alkylgruppe oder eine niedrige Alkoxygruppe; und Y bedeutet Sauerstoff oder eine Methylengruppe mit den Maßgaben, daß Y Sauerstoff ist, wenn R_2 eine Hydroxylgruppe und R_1 NH_2 ist, R_2 ist eine niedrige Alkylgruppe, R_3, R_4, R_5, R_6, R_7 und R_9 sind Wasserstoff, R_8 ist eine niedrige Alkylgruppe und R_{10} eine niedrige Alkoxygruppe, wenn Y eine Methylengruppe ist, welches Verfahren das Umsetzen einer durch die allgemeine Formel

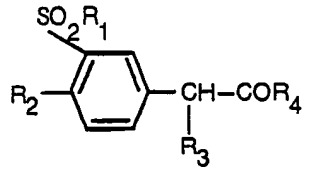


wiedergegebenen Verbindung, in welcher R Wasserstoff oder eine niedrige Alkylgruppe und R_1, R_2, R_4, R_5, R_6, R_7, R_8, R_9, R_{10} und Y wie oben definiert sind mit einem Halogenierungsmittel und dann, falls gewünscht, a) die Reduktion des halogenierten Produktes oder b) die Umsetzung des halogenierten Produktes mit einem niedrigen Alkohol oder Thiophenol und, falls gewünscht, die Oxidation des durch die Reaktion mit Thiophenol erhaltenen Produktes oder c) die Umsetzung des halogenierten Produktes mit einem alkalischen Stoff und dann die Reaktion des so erhaltenen Produktes mit Jodwasserstoff, einem niedrigen Alkohol oder Thiophenol und, falls gewünscht, die Oxidation des durch die Reaktion mit Thiophenol erhaltenen Produktes umfaßt.

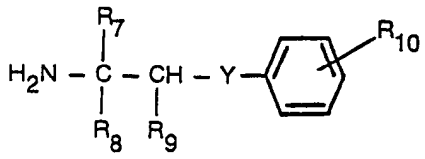
2. Ein Verfahren zur Herstellung eines neuen Sulfamoylphenäthylaminderivates, daß durch die allgemeine Formel



wiedergegeben ist, worin R_1 eine Aminogruppe oder eine mono- oder di-niedrig-Alkylaminogruppe bedeutet; R_2 bedeutet eine Hydroxylgruppe, eine niedrige Alkylgruppe oder eine niedrige Alkoxygruppe; R_3 bedeutet Wasserstoff, Halogen, eine niedrige Alkylgruppe, eine niedrige Alkoxygruppe, eine Phenylthiogruppe oder eine Phenylsulfinylgruppe; R_5 und R_6 sind Wasserstoff; R_4, R_7, R_8 und R_9 sind unabhängig voneinander unter Wasserstoff und niedrigen Alkylgruppen ausgewählt; R_{10} bedeutet Wasserstoff, eine niedrige Alkylgruppe oder eine niedrige Alkoxygruppe; und Y bedeutet Sauerstoff oder eine Methylengruppe mit den Maßgaben, daß Y Sauerstoff ist, wenn R_2 eine Hydroxylgruppe ist und R_1 NH_2 ist, R_2 ist eine niedrige Alkylgruppe, R_3, R_4, R_7 und R_9 sind Wasserstoff, R_8 ist eine niedrige Alkylgruppe und R_{10} eine niedrige Alkoxygruppe, wenn Y eine Methylengruppe ist, welches Verfahren die Kondensation einer Verbindung, welche durch die allgemeine Formel



wiedergegeben ist, mit einer Verbindung, welche durch die allgemeine Formel



wiedergegeben ist, worin R_1, R_2, R_3, R_4, R_7, R_8, R_9, R_{10} und Y wie oben definiert sind und dann die Reduktion des Kondensationsproduktes umfaßt.

3. Ein Verfahren nach Anspruch 1, worin R_3 Wasserstoff oder eine niedrige Alkylgruppe ist.

4. Ein Verfahren nach Anspruch 1 zur Herstellung von 5-[2-[2-(2-Äthoxyphenoxy)äthylamino]-2-methyläthyl}-2-methoxybenzolsulfonamid, welches Verfahren die Umsetzung von 5-[2-[2-(2-Äthoxyphenoxy)äthylamino]-1-hydroxy-2-methyläthyl}-2-methoxybenzolsulfonamid-Hydrochlorid mit dem Halogenierungsmittel Thionylchlorid umfaßt.

5. Ein Verfahren nach Anspruch 1 zur Herstellung von 2-Methoxy-5-[2-[2-(2-methoxyphenoxy)-äthylamino]-2-methyläthyl]benzolsulfonamid, welches Verfahren die Umsetzung von 2-Methoxy-5-[2-[2-(2-methoxyphenoxy)äthylamino]-1-hydroxy-2-methyläthyl]benzolsulfonamid mit dem Halogenierungsmittel Thionylchlorid umfaßt.

6. Ein Verfahren nach Anspruch 1 zur Herstellung von 5-[2-[2-(2-Methoxyphenoxy)äthylamino]-2-methyläthyl}-2-methylbenzolsulfonamid, welches Verfahren die Umsetzung von 5-[2-[2-(2-Methoxyphenoxy)äthylamino]-1-hydroxy-2-methyläthyl}-2-methylbenzolsulfonamid mit einem Halogenierungsmittel und die Reduktion des halogenierten Produktes unter Wasserstoff bei Verwendung eines Palladiumkohlekatalysators umfaßt.

7. Ein Verfahren nach Anspruch 1 zur Herstellung von 5-[2-[2-(2-Methoxyphenoxy)äthylamino]-äthyl}-2-methyl-benzolsulfonamid, welches Verfahren die Umsetzung von 5-[2-[2-(2-Methoxyphenoxy)-äthylamino]-1-hydroxy-2-äthyl}-2-methylbenzolsulfonamid mit dem Halogenierungsmittel Thionylchlorid umfaßt.

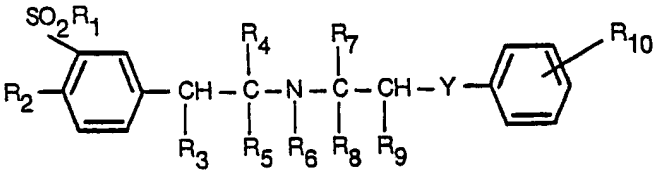
8. Ein Verfahren nach Anspruch 2 zur Herstellung von 2-Methoxy-5-[2-[2-(2-methoxyphenoxy)-äthylamino]-2-methyläthyl]-N-methylbenzolsulfonamid, welches Verfahren die Kondensation von 4-Methoxy-3-N-methylsulfamylphenylaceton mit 2-Methoxyphenoxyäthylamin umfaßt.

9. Ein Verfahren nach Anspruch 2 zur Herstellung von 2-Methoxy-5-[2-[2-(2-methoxyphenoxy)-äthylamino]-2-methyläthyl]-N,N-dimethylbenzolsulfonamid, welches Verfahren die Kondensation von 4-Methoxy-3-N,N-dimethylsulfamylphenylaceton mit 2-Methoxyphenoxyäthylamin umfaßt.

10. Ein Verfahren nach einem vorhergehenden Anspruch, welches eine zusätliche Stufe zur Umwandlung des Reaktionsproduktes in die Salzform umfaßt.

Revendications pour les Etats contractants: BE CH DE FR GB IT LI LU NL SE

1. Un dérivé de la phénéthylamine substitué par un groupe sulfamoyle représenté par la formule générale



dans laquelle R_1 représente un groupe amino ou un groupe mono ou di-(alcoyle inférieur)-amino; R_2 représente un groupe hydroxyle, un groupe alcoyle inférieur, ou un groupe alcoxy inférieur; R_3 représente un hydrogène, un halogène, un groupe alcoyle inférieur, un groupe alcoxy inférieur, un groupe phénylthio, ou un groupe phénylsulfinyle; R_4, R_5, R_6, R_7, R_8 et R_9 sont choisis indépendamment à partir de l'hydrogène et des groupes alcoyles inférieurs; R_{10} représente un hydrogène, un groupe alcoyle inférieur ou un groupe alcoxy inférieur; et Y représente un oxygène ou un groupe méthylène avec les réserves que Y est un oxygène lorsque R_2 est un groupe hydroxyle, et R_1 est NH_2, R_2 est un groupe alcoyle inférieur, R_3, R_4, R_5, R_6, R_7, et R_9 sont des hydrogènes, R_8 est un groupe alcoyle inférieur et R_{10} un groupe alcoxy inférieur quand Y est un groupe méthylène; ou un sel de celui-ci.

2. Un composé selon la revendication 1 dans lequel R_3 est un hydrogène ou un groupe alcoyle inférieur.

3. Le 5-{2-[2-(2-éthoxyphénoxy)éthylamino]-2-méthyléthyl}-2-méthoxybenzènesulfonamide.

4. Le 2-méthoxy-5-{2-[2-(2-méthoxyphénoxy)éthylamino]-2-méthyléthyl}benzenesulfonamide.

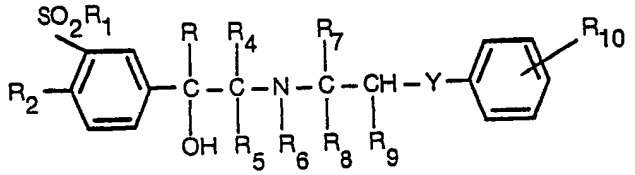
5. Le 5-{2-[2-(2-méthoxyphénoxy)éthylamino]-2-méthyléthyl}-2-méthylbenzènesulfonamide.

6. Le 5-{2-[2-(2-méthoxyphénoxy)éthylamino]éthyl}-2-méthylbenzénesulfonamide ou le 2-méthoxy-5-{2-[2-(2-méthoxyphénoxy)éthylamino]-2-méthyléthyl}-N-méthylbenzènesulfonamide ou le 2-méthoxy-5-[2-[2-(2-méthoxyphénoxy)éthylamino]-2-méthyléthyl}-N,N-diméthylbenzènesulfonamide.

7. Un sel d'un composé selon l'une quelconque des revendications 3 à 6.

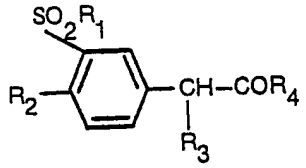
8. Une composition pharmaceutique contenant un composé selon l'une quelconque des revendications précédentes et un excipient.

9. Un procédé de production d'un composé selon la revendication 1 qui consiste à faire réagir un composé représenté par la formule générale

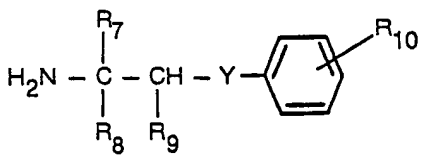


dans laquelle R représente un hydrogène ou un groupe alcoyle inférieur et R_1, R_2, R_4, R_5, R_6, R_7, R_8, R_9, R_{10} et Y sont tels que définis dans la revendication 1 avec un agent d'halogénation et ensuite si désiré a) en réduisant le produit halogéné; ou b) en faisant réagir le produit halogéné avec un alcool inférieur ou du thiophénol et, si désiré, en oxydant le produit obtenu par la réaction avec le thiophénol; ou c) en faisant réagir le produit halogéné avec un matériau alcalin et en faisant réagir ensuite le produit ainsi obtenu avec l'acide iodhydrique, un alcool inférieur, ou du thiophénol et, si désiré, en oxydant le produit obtenu par le réaction avec le thiophénol.

10. Procédé de production d'un composé selon la revendication 1, dans lequel R_5 et R_6 sont des hydrogènes, qui consiste à condenser un composé représenté par la formule générale



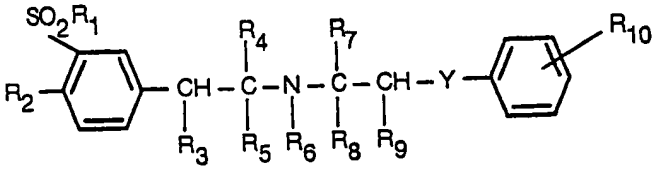
avec un composé représenté par la formule générale



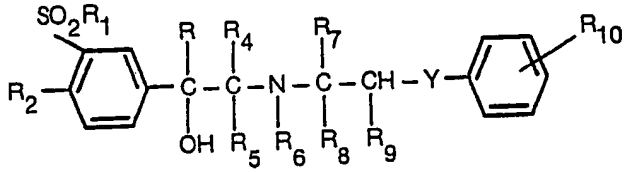
dans laquelle R_1, R_2, R_3, R_4, R_7, R_8, R_9, R_{10} et Y sont tels que définis dans la revendication 1 et en réduisant ensuite le produit condensé.

Revendications pour l'Etat contractant: AT

1. Un procédé pour la production 'un nouveau dérivé de la phénéthylamine substitué par un groupe sulfamoyle représenté par la formule générale

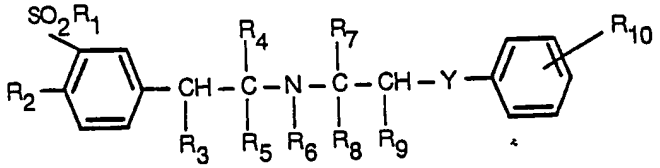


dans laquelle R_1 représente un groupe amino ou un groupe mono- ou di-(alcoyle inférieur)-amino; R_2 représente un groupe hydroxyle, un groupe alcoyle inférieur, ou un groupe alcoxy inférieur; R_3 représente un hydrogène, un halogène, un groupe alcoyle inférieur, un groupe alcoxy inférieur, un groupe phénylthio, ou un groupe phénylsulfinyle; R_4, R_5, R_6, R_7, R_8 et R_9 sont choisis indépendamment parmi l'hydrogène et les groupes alcoyles inférieurs; R_{10} représente un hydrogène, un groupe alcoyle inférieur ou un groupe alcoxy inférieur; et Y représente un oxygène ou un groupe méthylène avec les réserves que Y est un oxygène lorsque R_2 est un groupe hydroxyle, et R_1 est NH_2, R_2 est un groupe alcoyle inférieur, R_3, R_4, R_5, R_8, R_7 et R_9 sont des hydrogènes, R_8 est un groupe alcoyle inférieur et R_{10} un groupe alcoxy inférieur quand Y est un groupe méthylène, ce procédé consistant à faire réagir un composé représenté par la formule générale

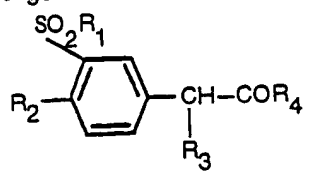


dans laquelle R représente un hydrogène ou un groupe alcoyle inférieur et R_1, R_2, R_4, R_5, R_6, R_7, R_8, R_9, R_{10} et Y sont tels que définis ci-dessus avec un agent d'halogénation et ensuite si désiré a) à réduire le produit halogéné; ou b) à faire réagir le produit halogéné avec un alcool inférieur ou du thiophénol et, si désiré, à oxyder le produit obtenu par la réaction avec du thiophénol; ou c) à faire réagir le produit halogéné avec un matériau alcalin et à faire réagir ensuite le produit ainsi obtenu avec l'acide iodhydrique, un alcool inférieur, ou du thiophénol et, si désiré, à oxyder le produit obtenu par la réaction avec le thiophénol.

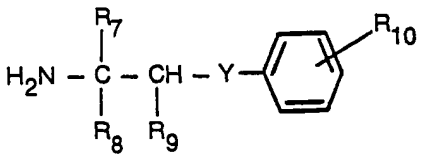
2. Un procédé pour la production d'un nouveau dérivé de la phénéthylamine substitué par un groupe sulfamoyle représenté par la formule générale



dans laquelle R_1 représente un groupe amino ou un groupe mono- ou di-(alcoyle inférieur)-amino; R_2 représente un groupe hydroxyle, un groupe alcoyle inférieur, ou un groupe alcoxy inférieur; R_3 représente un hydrogène, un halogène, un group alcoyle inférieur, un groupe alcoxy inférieur, un groupe phénylthio, ou un groupe phénylsulfinyle; R_5 et R_6 sont un hydrogène; R_4, R_7, R_8 et R_9 sont choisis indépendamment parmi l'hydrogène et les groupes alcoyles inférieurs; R_{10} représente un hydrogène, un groupe alcoyle inférieur ou un groupe alcoxy inférieur; et Y représente un oxygène ou un groupe méthylène avec les réserves que Y est un oxygène lorsque R_2 est un groupe hydroxyle, et R_1 est NH_2, R_2 est un groupe alcoyle inférieur, R_3, R_4, R_7 et R_9 sont des hydrogènes, R_8 est un groupe alcoyle inférieur et R_{10} un groupe alcoxy inférieur quand Y est un groupe méthylène, ce procédé consistant à condenser un composé représenté par la formule générale



avec un composé représenté par la formule générale



dans lesquelles R_1, R_2, R_3, R_4, R_7, R_8, R_9, R_{10} et Y sont tels que définis ci-dessus et en réduisant ensuite le produit de condensation.

3. Un procédé selon la revendication 1 dans lequel R_3 est un hydrogène ou un groupe alcoyle inférieur.

4. Un procédé selon la revendication 1 pour produire le 5-{2-[2-(2-éthoxyphénoxy)éthylamino]-2-méthyléthyl}-2-méthoxybenzènesulfonamide, procédé qui consiste à faire réagir le chlorhydrate de 5-{2-[2-(2-éthoxyphénoxy)éthylamino]-1-hydroxy-2-méthyléthyl}-2-méthoxybenzènesulfonamide avec un agent halogénant le chlorure de thionyle.

5. Un procédé selon la revendication 1 pour produire le 2-méthoxy-5-{2-[2-(2-méthoxyphénoxy)-éthylamino]-2-méthyléthyl}benzènesulfonamide, procédé qui consiste à faire réagir le 2-méthoxy-5-{2-[2-(2-méthoxyphénoxy)éthylamino]-1-hydroxy-2-méthyléthyl}benzènesulfonamide avec un agent halogénant le chlorure de thionyle.

6. Un procédé selon la revendication 1 pour produire le 5-{2-[2-(2-méthoxyphénoxy)éthylamino]-2-méthyléthyl}-2-méthylbenzènesulfonamide, procédé qui consiste à faire réagir le 5-{2-[2-(2-méthoxyphénoxy)éthylamino]-1-hydroxy-2-méthyléthyl}-2-méthylbenzènesulfonamide avec un agent halogénant et à reduire le produit halogéné sous hydrogène en utilisant le carbone-palladium comme catalyseur.

7. Un procédé selon la revendication 1 pour produire le 5-{2-[2-(2-méthoxyphénol)éthylamino]-éthyl}-2-méthylbenzènesulfonamide procédé qui consiste à faire réagir le 5-{2-[2-(2-méthoxyphénoxy)-éthylamino]-1-hydroxy-2-éthyl}-2-méthylbenzènesulfonamide avec un agent halogénant le chlorure de thionyle.

8. Un procédé selon la revendication 2 pour produire le 2-méthoxy-5-{2-[2-(2-méthoxyphénoxy)-éthylamino]-2-méthyléthyl}-N-méthylbenzènesulfonamide, procédé qui consiste à condenser la 4-méthoxy-3-N-méthylsulfamoyl-phényl-acétone avec la 2-méthoxyphénoxyéthylamine.

9. Un procédé selon la revendication 2 pour produire le 2-méthoxy-5-{2-[2-(2-méthoxyphénoxy)-éthylamino]-2-méthyléthyl}-N,N-diméthylbenzènesulfonamide, procédé qui consiste à condenser la 4-méthoxy-3-N,N-diméthylsulfamoyl-phényl-acétone avec la 2-méthoxyphénoxyéthylamine.

10. Un procédé selon l'une quelconque des revendications précédentes qui comporte le stade additionnel qui consiste à convertir le produit de la réaction sous forme d'un sel.